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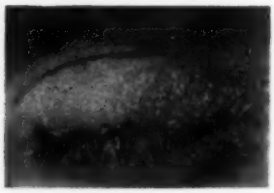

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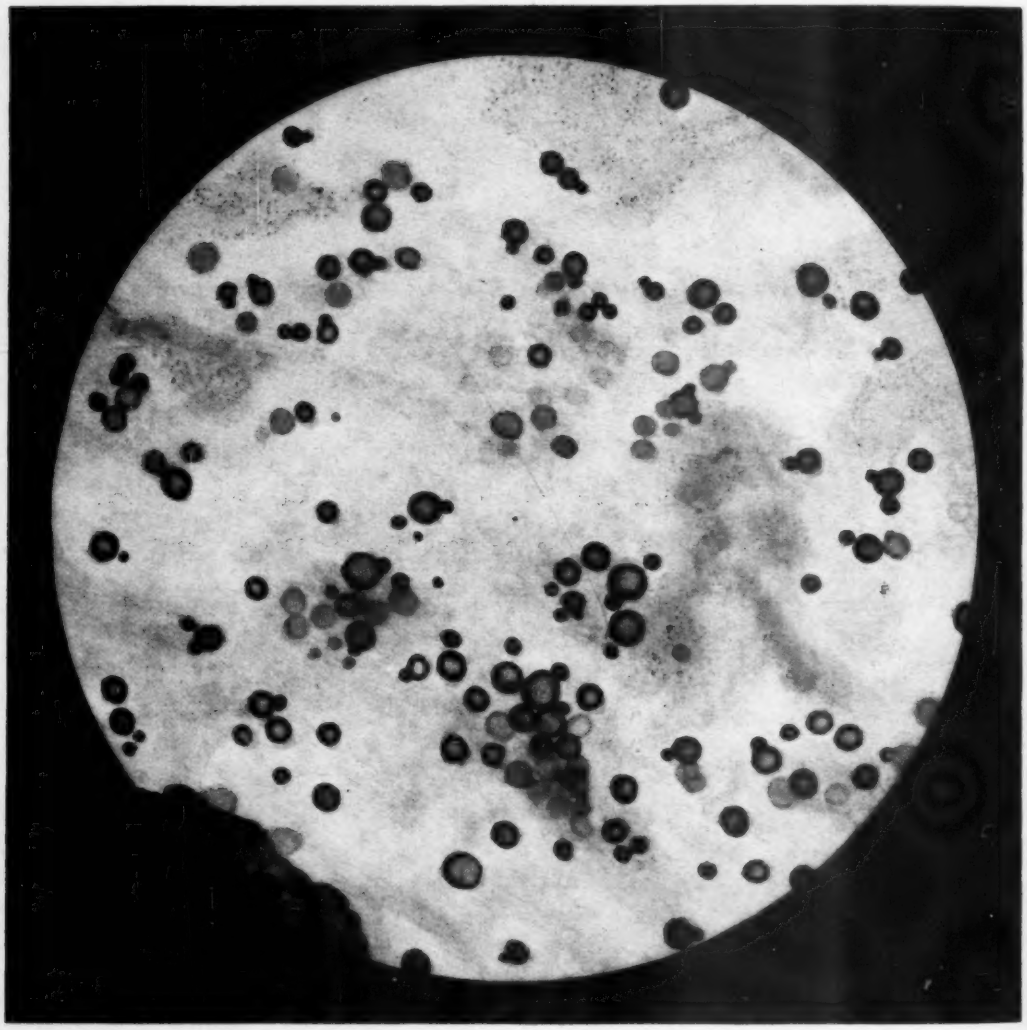

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OBSERVATIONS ON *PITYROSPORUM OVALE* IN SEBORRHEIC BLEPHARITIS AND CONJUNCTIVITIS*

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INTRODUCTION

Pityrosporum ovale, a yeastlike fungus as yet unclassified, was first described in 1874 by Malassez[1] who considered it to be the cause of seborrheic dermatitis. Although P. ovale is constantly present in this disease, there is still a difference of opinion among dermatologists as to whether its role is pathogenic or purely saprophytic. Etiologic studies have been handicapped by the fact that pure cultures of P. ovale have been obtained only with great difficulty, and by the fact that no experimental animal has been shown to be truly susceptible to seborrheic dermatitis. A number of inoculation experiments on human beings have been reported but the results have always been in doubt because of the possibility of error in the identification of the organism and in the interpretation of the induced skin lesions.

Seborrheic dermatitis, whose major localization is the scalp (seborrhea capitis, pityriasis capitis), has long been known to affect the eyebrows and eyelids, seborrheic blepharitis being one of the principal types of lid-margin infection. In 1938, Kile and Engman[2] reported finding varying numbers of P. ovale in scrapings from the lid margins of 21 of a series of 24 patients with blepharitis. In many instances large numbers of the organism were seen, even in the presence of secondary pyogenic infection. Nearly every one of these patients also had pityriasis of the scalp. As a result of numerous attempts to cultivate P. ovale from the lid margins of each of 10 of these patients, cultivation was obtained in three. Scales from the eyelids of six patients were used to inoculate excoriations on the chest. In two instances there were positive reactions consisting of scaliness, slight erythema, and a subsequent browning of the skin. The lid margins of five rabbits were rubbed with P. ovale culture without result.

In 1945, one of us (P. T.)[3] reported finding P. ovale in a high percentage of scrapings from cases of blepharitis and noted the close correlation between the

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clinical manifestations of seborrheic blepharitis and the demonstration of the organism. He suggested that lid-margin scrapings were of value in the diagnosis of seborrheic blepharitis and of even greater value, as a guide to therapy, in evaluating the importance of the seborrheic factor in cases showing pyogenic infection.

The present study was undertaken in an attempt to cast further light on the role of P. ovale in seborrheic blepharitis and in the conjunctivitis and keratitis which sometimes accompany it. It is concerned with the morphology of the organism, its cultivation, its frequency in external inflammations of the eye, and its pathogenicity for man and animals.

Isolation of P. ovale

All reports in the literature indicate that P. ovale is extremely difficult to cultivate. Since it does not have absolutely distinctive morphologic characteristics and fails to produce specific lesions on animal inoculation, it has been difficult to prove that fungi isolated from the scales of seborrheic dermatitis were indeed P. ovale. Benham[4] has recently reported the cultivation of the organism and has defined its cultural characteristics. From her work it would seem that identification of the organism in culture is based essentially on its microscopic morphology, on its colony appearance and rate of growth, and, most importantly, on its lipophilic properties.

Method

In the studies reported here, the following media were employed: (1) Sabaraud's dextrose agar (Difco), (2) wort agar (Difco), and (3) wort agar plus 1.5-percent oleic acid. The dehydrated wort agar was used in a concentration of 6 percent instead of the 5 percent recommended by the manufacturer, because the latter produced too soft a medium after the addition of oleic acid.

Cultures from blepharitis subjects were made by removing the macroscopic scales from the lids with a sterile platinum wire or spatula and introducing them directly to the surface of the agar plate. After the scales had been removed, the lids were rubbed with a sterile cotton swab which was then streaked onto the unused portion of the agar plate. In the cases in which no scales were evident, the swab method only was employed. Plates were sealed with wide rubber bands, incubated at 37°C., and examined daily for growth. As soon as any colony growth whatever appeared which resembled P. ovale microscopically, the colony was streaked out on the plate with a wire loop. A more luxuriant growth was thus obtained in a shorter time than would otherwise have been possible.

Cultures of dandruff were made by having the patient brush his hair with his fingers over an exposed plate. The plates were incubated at 37°C. and when growth first appeared on the scales, or around them, it was streaked out.

From cases of seborrheic dermatitis, scales were obtained with a platinum loop or spatula and implanted directly onto the surface of the culture plate.

Isolation from blepharitis. A total of 24 cases of blepharitis showing yeastlike bodies suggesting P. ovale in lid-margin scrapings were studied for the presence of P. ovale. On Sabaraud's medium, which was used in 16 of the 24 cases, staphylococci were recovered invariably and in several instances there were also other cocci and Gram-positive rods. On this medium, staphylococci, although not abundant, were by no means inhibited. A yeast which was not P. ovale was isolated from one case. Contaminating molds were not uncommon.

On wort agar, which was used in all 24 cases, Gram-positive cocci were found

in a few cases and yeasts in four. No P. ovale were isolated. Contaminating molds, particularly *Penicillium, Aspergillus,* and *Alternaria,* were common.

Wort agar containing 1.5-percent oleic acid was also used in all 24 cases. No bacteria grew on this medium, but yeasts were isolated from six cases. Molds were uncommon although their rapid overgrowth in three cases necessitated the discarding of plates. Organisms believed to be P. ovale were isolated from five cases, that is, 5 out of 24, or 21 percent. Three of these isolations were subcultured and maintained through several generations. The other two were never successfully isolated in pure culture and were lost due to contaminating molds. The first colonies of the organism appeared in from 4 to 7 days.

In a subsequent culture study made in San Francisco, P. ovale was isolated in pure culture on wort agar containing oleic acid from 1 of 5 cases of seborrheic blepharitis from which isolation was attempted and has been maintained in pure culture through 10 transfers.

Isolation from dandruff (pityriasis capitis). Six cases of dandruff, in which P. ovale-like organisms were readily demonstrable by microscopic examination of the scales, were cultured on wort agar containing oleic acid. Isolation of the organism was accomplished in 4 of the 6 cases.

Isolation from seborrheic dermatitis. P. ovale-like organisms were found in the epidermal scales of three patients with seborrheic dermatitis of the face. The scales were removed and planted on wort agar containing oleic acid. Typical P. ovale were isolated from all three cases.

Properties of P. ovale

The following criteria were used for the identification of the organism in this study: (1) Microscopic morphology, which included typical bottle forms as described in the literature. (2) Colony morphology; that is, the slow-growing colonies of typical appearance and color as described by Benham.[4] (3) Lipophilic properties as determined by (a) failure to grow either in primary isolation or in subculture in media not containing oleic acid but readiness to grow in media containing it, and (b) growth characteristics in Benham's synthetic medium.[5] This is a clear aqueous solution of inorganic salts and glucose to which oleic acid is added. The lipophilic organisms produce an opacity of the oil globules, by growing in and around them, and leave the aqueous portion clear. Nonlipophilic organisms produce a marked turbidity in the aqueous portion and the oil globules remain clear and translucent. (4) Confirmation of the isolation (3 cases) by Dr. Rhoda Benham of Columbia University.

The cultural characteritsics of the organisms isolated in this series coincided with those described by other workers, including Benham[4] and Moore and associates.[6] The bottle or flask-shaped forms were typical and characteristic. While these forms predominated in cultures, other forms were also found, including dumb-bell shaped, elongated, oval, lemon-shaped, pear-shaped, and budding forms. The size of the oval and elongated forms varied from 2 to 7 microns in length and from 1½ to 2½ microns in width. The organisms had a definite tendency to form clumps.

The first colonies appeared in from 4 to 7 days after inoculation but subcultures grew more rapidly, colonies appearing in from 2 to 5 days. A cheesy odor was characteristic. Typical colonies were small (½ mm. in diameter), convex, granular, feather-edged, and light tan in color. The color darkened with age and the oily surface characteristic of young colonies became dry and powdery. Aging also pro-

duced corrugation and wrinkling of the colony which became hard, brittle, compact, and impossible to emulsify. On subculture, giant colonies as large as 12 mm. in diameter developed after two weeks' growth. Some strains became nonviable after multiple subcultures but three strains survived 15 subcultures. These three were sent to New York to Dr. Rhoda Benham who reported that they were identical with the strains of P. ovale isolated by her.

P. OVALE IN LID-MARGIN SCRAPINGS

Figure 1 illustrates the usual appearance of the organism in lid-margin scrapings. There was considerable variation in morphology, but spherical cells, both large and small, and often with budding, were the most common forms. Flask or bottle forms, so common on the scalp, were rarely seen in preparations from the lid margin. The smallest cell observed was about 2 microns in diameter and the largest about 11 microns. It was noted on repeated examination that in the same individual there would be a preponderance of spherical budding forms on the lid margins and a preponderance of oval and flask-shaped forms on the scalp. In a certain number of cases, however, almost 100 percent of the forms on the lid margins were flask-shaped. No clear relationship between the type of clinical blepharitis and the preponderance of either spherical or oval forms was apparent. Moore and his associates,[6] on the other hand, stated that small, ovoid, budding forms were characteristic of acute, rapidly spreading infections, that both ovoid and spherical cells were seen in active subacute infections, and that in chronic or quiescent lesions many large, thick-walled, resting cells, as well as both ovoid and spherical cells, were to be found.

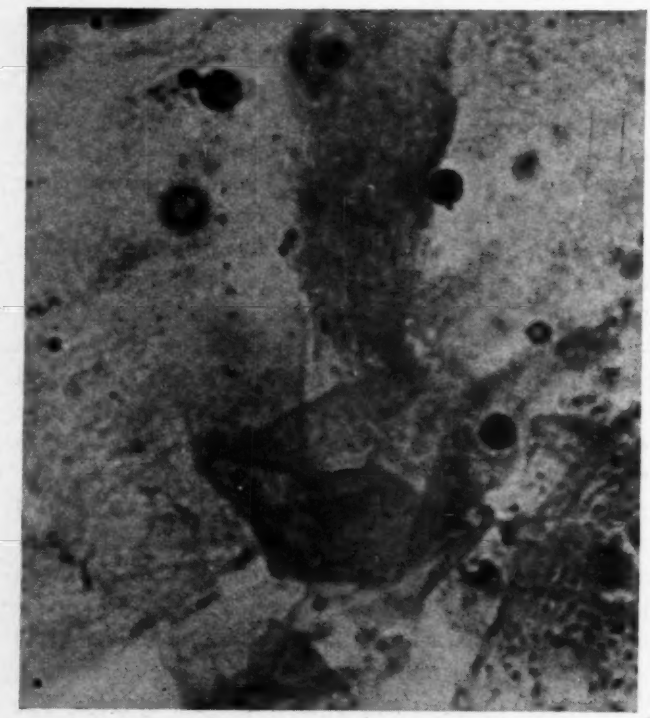

Fig. 1 (Gots, Thygeson, and Waisman). *Pityrosporum ovale* in lid-margin scrapings from a case of typical seborrheic blepharitis. Giemsa stain. (Magnification ×2,400.)

In this study budding yeast forms morphologically like P. ovale were found in 100 percent of 143 cases of clinically typical seborrheic blepharitis. As previously reported by one of us, typical seborrheic blepharitis (fig. 2) is squamous in type, with large, greasy scales, and is associated with seborrheic dermatitis of the scalp and often of the brows. While this is the more common form, the disease may also appear as a squamous blepharitis with dry, small scales and hyperemic lid margins. Excluded from this study were a considerable number

of cases complicated by pathogenic staphylococci.

The organisms were most numerous in scrapings from those portions of the lid margins which showed the greatest inflammation and, as also reported by Moore and associates,[6] they were almost always present in the upper portion of the hair follicles of the cilia. They could be seen adhering to the shafts of cilia removed and examined microscopically.

The effect of therapy upon the organism in lid-margin scrapings was significant. The customary treatment for seborrheic blepharitis has been twice-weekly applications of silver nitrate to the lid margins and twice-daily applications of an ointment consisting of 1-percent ammoniated mercury and 1-percent salicylic acid in petrolatum. Under this treatment there was rapid disappearance of the organisms from scrapings, but if treatment was interrupted prematurely for any length of time, the organisms inevitably recurred. Moreover, when apparently healed cases suffered recurrences, P. ovale invariably reappeared in lid margin scrapings.

Treatment with 5-percent sulfathiazole ointment or penicillin ointment alone did not significantly affect the number of P. ovale in scrapings. This paralleled the lack of therapeutic effect of these two preparations on pure seborrheic blepharitis.

Sensitization to P. ovale extract

An extract of P. ovale culture, prepared according to the method employed in the preparation of trichophytin,[7] was used for sensitivity studies in 46 individuals suffering from seborrheic blepharitis in which P. ovale was demonstrated in scrapings. All cases also had scalp infection of one degree of severity or another. The test was made by the injection of 0.1 cc. of the extract intradermally into the skin of the forearm or upper arm. Readings were made in one hour and again in 24 and 48 hours. No immediate reactions of significance were noted and only 5 of the 46 individuals showed delayed reactions believed to be significant. In these there was a tuberculinlike reaction and in two of the cases the area of erythema was six inches or more in diameter. Of these five positive cases, three had severe seborrheic blepharitis with severe conjunctivitis and keratitis. These were the only severe cases in the entire group of 46 individuals tested for skin sensitivity.

Sixteen individuals without seborrheic blepharitis, and without obvious scalp infection or history of seborrheic dermatitis, were also tested. In these there were no significant reactions, immediate or delayed.

Animal and Human experimentation

Animal subjects

Transmission experiments with scrapings from seborrheic blepharitis. A search of the literature disclosed no record of the production of a typical seborrheic dermatitis or blepharitis in animals with scrapings from the human disease, and no record of the occurrence of the disease spontaneously in animals. In a rather wide experience with laboratory animals, including monkeys, apes, dogs, guinea pigs, rabbits, rats, and mice, we do not recall ever having seen any skin lesion suggestive of seborrheic dermatitis or blepharitis. It seemed worthwhile, however, to attempt transmission of the disease with scrapings from seborrheic blepharitis. For this purpose 12 cases were chosen in which P. ovale was present in large numbers in the epithelial scrapings. Inoculation by light scarifica-

tion with a platinum spatula was made directly from the lesions. The skin, lid margins, and conjunctivas were inoculated simultaneously in a total of 18 rabbits and 21 guinea pigs. In no instance did an infection resembling seborrheic dermatitis result. A mild, self-limited, scaly dermatitis of short duration developed in five rabbits but could not be considered significant. Except for transient hyperemia of the conjunctiva after inoculation, no conjunctival changes were noted in either rabbits or guinea pigs.

Transmission experiments with P. ovale culture. Skin. Two rabbits were inoculated by rubbing P. ovale organisms, obtained from heavy agar-plate growth, into a scarified area on one side of each rabbit. As a control the other side was inoculated similarly with a nonpathogenic yeast (Saccharomyces).

RABBIT 1. There was nothing of note until the sixth day when a definite scaliness appeared on the side inoculated with P. ovale. The control side also tended toward scaliness but the scales were firm and intact in contrast to the loose, flaky scales on the side inoculated with P. ovale. Methylene-blue mounts of these scales were negative and no organisms were obtained from them in culture. Examinations were made periodically. The scaliness persisted and on the 14th day, scales which were cultured yielded an organism which was at first thought to be P. ovale. The similarity was striking but further studies showed that it was not P. ovale as it grew readily in the absence of fats and developed mycelia. The scaly condition disappeared spontaneously and on the 24th day the rabbit appeared to be normal.

RABBIT 2. There was nothing of note until the sixth day when a thick, brownish yellow encrustation developed at the site of the P. ovale inoculation. The appearance of this lesion corresponded with the description of the lesions on rabbits given by Moore and associates.[6] The control site presented a few fine, thin crusts which were not as heavy nor as thick as those on the inoculated side and may well have been due to the scabbing over induced by the scarification. The crusts from the side inoculated with P. ovale were removed and P. ovale forms were found in methylene-blue mounts and were grown successfully in culture. In this experiment there was no doubt as to the organism's identity. The crustlike appearance rapidly disappeared and on the 10th day was replaced by a flaky, loose scaliness. No organisms were demonstrated in these scales nor isolated in culture. By the 19th day the area appeared normal. No spreading occurred.

In an effort to determine the effect of scarification alone, the skin was scarified as before but no organisms were introduced. A slight scaliness with a few fine crusts appeared. This lesion was comparable to that produced by the control inoculation of Rabbit 2. No loose, flaky scaliness developed.

Thirty days after the inoculation of Rabbit 2, identical inoculations were made at the same sites. The reactions were the same as in the first experiments and P. ovale forms were found in the scales. There was no evidence of sensitivity to the previous inoculation. No positive cultures were obtained, but in this connection it should be borne in mind that the culturing of the rabbit scales was extremely difficult due to the profusion of contaminating molds; the one positive culture obtained in the first experiment was barely saved. Before the second inoculations were made the skin of one of the areas was rubbed with oleic acid. This was done to see if the "take" would be

better. The oleic acid had no apparent effect on the type or degree of response.

Eye. The upper lid of the eye of a rabbit was rubbed with growth from a culture of P. ovale. A control yeast was rubbed on the lid of the other eye. No changes occurred until the ninth day when a macroscopic scaliness appeared along the margin of the lid inoculated with P. ovale. Scrapings from this lesion showed many P. ovale forms and identical forms were demonstrated continuously in scrapings taken on the 11th, 19th, and 21st days. No organisms were found in scrapings from the control eye. Scrapings from the six eyelids of three normal rabbits were also negative. In no instance was P. ovale isolated in culture. The scaliness diminished gradually but was still evident after 34 days. No spreading occurred. In comparison with the conjunctiva of the control eye, the conjunctiva of the eye inoculated with P. ovale was mildly hyperemic.

Ear. P. ovale were also inoculated directly, without scarification, onto the ear of a rabbit, and a control yeast onto the other ear. A flaky, loose scaliness developed on the 10th day on the ear inoculated with P. ovale. The control side presented a scaliness which was firm and intact. Examination of normal rabbits' ears revealed the same type of firm, intact, scaly surface. Scales from the P. ovale side were loose and profuse, particularly in the area of inoculation. No spreading occurred. P. ovale-like organisms were readily demonstrated in methylene-blue mounts but no positive cultures were obtained. The scaliness disappeared spontaneously after the third week.

The same place on the same ear was again inoculated 30 days after the first inoculation. Again a loose, flaky scaliness appeared but this time there was also a marked erythema which may possibly have been a manifestation of sensitivity produced by the previous inoculation.

Human subjects

Strips of gauze containing growth from a culture of P. ovale were placed on the backs of two human volunteers and left in situ for 24 hours.

Patient 1. Results negative after one week.

Patient 2. On the fifth day an area of dry erythema and dry superficial scaling was evident. The lesion did not resemble typical seborrheic dermatitis. The area affected corresponded closely to the application site. No spreading occurred in three days. P. ovale-like organisms were found in methylene-blue mounts of scales. No cultures were made.

Other yeastlike organisms from blepharitis

A total of 11 yeastlike organisms, other than P. ovale, were isolated from 8 of the 24 cases of blepharitis subjected to culture study. These all appeared similar microscopically and culturally. The colony growth was white and pasty, turning tan and brown with age. There was a typical yeasty odor. Growth occurred readily on Sabaraud's medium, wort agar, and blood-agar plates. In Benham's synthetic medium[5] growth occurred in the aqueous component, the oil globules remaining clear. Microscopic examination revealed a preponderance of oval forms. Growth first appeared in from 2 to 7 days. After two weeks giant colonies of four strains developed the characteristic "eruption" surface due to gas formation. No ascospores were demonstrated on carrot media. Mycelium formation was studied on corn-meal agar by slide-culture technique. Seven of the strains formed mycelia. These were considered to be members of the Monilia-Mycotorula

group, and the four which did not produce mycelia to be members of the Cryptococcus group. No further identification could be made.

The occurrence of these yeasts in lid-margin cultures raises the question of the identification of P. ovale in lid margin scrapings. Can other yeasts simulate P. ovale? In an effort to clarify this point, the correlation between the appearance of P. ovale-like forms in lid-margin scrapings and the growth of yeasts on Sabaraud's medium, wort agar, and blood-agar plates, was studied in a series of 12 cases. All ordinary yeasts grow readily on these media and, if present in any numbers on the lid margin, would make profuse growth on culture. This was not the case, however, since never more than two or three colonies of yeast developed on these media from any one of the dozen cases, even though yeastlike forms were numerous in scrapings. It is our belief, therefore, that the sporadic yeasts isolated were air-borne contaminants.

Discussion

In looking for a relationship which might be analogous to that of P. ovale in seborrheic blepharitis and its secondary conjunctivitis and keratitis, one inevitably turns to a consideration of the role of *Corynebacterium xerosis* in xerophthalmia. It will be recalled that the xerosis bacillus, found constantly in xerophthalmia, was originally described as the cause of the disease. Attempts to reproduce xerophthalmia with pure cultures of the diphtheroid invariably failed, however, and the disease was eventually shown to be due to avitaminosis A. Is it possible that P. ovale may play the same saprophytic role in seborrheic blepharitis?

According to the evidence available, the following important differences seem to obtain: (1) Seborrheic dermatitis, unlike xerophthalmia, is almost undoubtedly infectious even though there is as yet no positive proof; (2) P. ovale, unlike C. xerosis, is not entirely devoid of pathogenicity for animals; and (3) C. xerosis is a saprophyte which will grow on almost any medium; whereas P. ovale, like many pathogens, is fastidious in its growth requirements. As a matter of fact, it is extremely difficult to isolate P. ovale and maintain it in pure culture as it is unable to grow in the absence of lipids. Its growth requirements would be more readily supplied by a parasitic existence via the naturally occurring fatty acids. For these reasons it seems unlikely that P. ovale could play a purely saprophytic role.

Etiologic studies in seborrheic dermatitis have been made extremely difficult by the lack of a suitable experimental animal. To our knowledge the direct transmission of seborrheic dermatitis to animals has not been obtained and certainly no one has ever produced with lid-margin scrapings the clinical picture of seborrheic blepharitis and its associated conjunctivitis and keratitis. Even human inoculations have not been entirely satisfactory. Thus it would seem to be almost impossible to fulfill Koch's postulates in this disease.

If Koch's postulates cannot be fulfilled, what are the possibilities for determining etiology? If P. ovale is the etiologic agent it should satisfy the following conditions: (1) It should produce the same results in animal and human inoculation experiments as are obtainable with tissue from seborrheic dermatitis. (2) It should be found consistently in the lesions of the disease. (3) It should be absent, unless a carrier state should exist, from the healed lesions.

As reported in this study, P. ovale produced a mild dermatitis and conjunctivitis in the rabbit comparable to that produced by scrapings from seborrheic blepharitis;

it was found consistently in the lesions of the disease; and, with a few exceptions only, it was absent in clinically normal lids. The demonstration of skin sensitivity to P. ovale extract in certain individuals indicates, moreover, that the organism produces inflammation irrespective of its role in seborrheic dermatitis.

Noteworthy in this study was the occurrence, in rare instances, of a very severe conjunctivitis and keratitis in association with seborrheic blepharitis. Eight such cases are reported and in each P. ovale was present in enormous numbers in lid-margin scrapings (fig. 3) and in lesser numbers in the conjunctival secretion (fig. 4). In these cases there were no demonstrable pathogenic staphylococci or other pathogens. The occurrence of a skin reaction to P. ovale extract in the three cases tested was significant and suggests the possibility that the conjunctival and corneal lesions were allergic in nature.

Therapeutic studies in seborrheic blepharitis yielded data of interest in connection with P. ovale. In the 56 cases in which lid margin scrapings were examined repeatedly during the course of treatment, there was a definite correlation between clinical improvement and reduction in the number of P. ovale. When the disease recurred in patients who had been rendered symptom free by therapy, there was invariably a recurrence of P. ovale in the scrapings.

Summary and Conclusions

1. Seborrheic dermatitis of the eyelids is a common external disease. Ordinarily mild and almost symptomless when not secondarily infected, the disease in its pure form is occasionally associated with a severe conjunctivitis and keratitis. The only constant bacteriological finding in the disease is the presence of *Pityrosporum ovale.*

2. First described in 1874, this as yet unclassified yeastlike organism has been incompletely studied and its role in seborrheic dermatitis remains unsettled. Clinical seborrheic dermatitis does not occur naturally in animals and animal

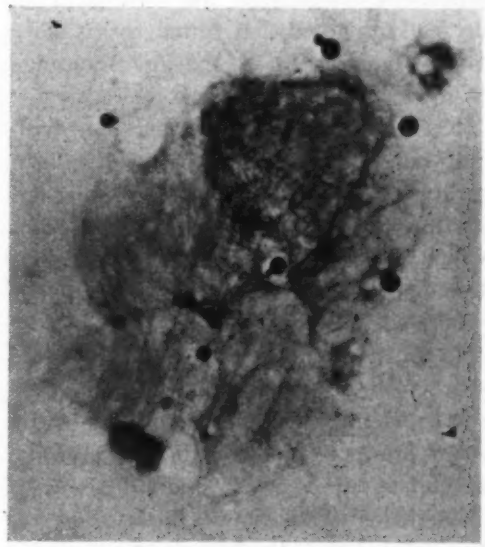

Fig. 4 (Gots, Thygeson, and Waisman). *Pityrosporum ovale* in conjunctival exudate from a case of severe seborrheic blepharitis with associated conjunctivitis and keratitis. Giemsa stain (Magnification ×1,150).

inoculations with P. ovale have failed to reproduce the disease. The few human inoculations recorded have been inconclusive. Difficulties concerned with the isolation of the organism in pure culture and with the recognition of the experimental disease make it impossible to determine on the basis of published reports whether the organism occurs in the lesions of seborrheic dermatitis as a saprophyte or is concerned etiologically.

3. The occurrence of P. ovale in scrapings from 100 percent of 143 cases of clinically recognizable seborrheic dermatitis of the eyebrows and eyelids is reported. The organism was isolated in pure culture with difficulty and only on media containing fatty acid, such as oleic-acid-

wort-agar medium. In scrapings the organisms usually appeared in moderate numbers in mild cases and in enormous numbers in severe cases.

4. The morphologic and cultural aspects of the organism isolated from seborrheic blepharitis are described in detail. It is noted that round forms were more common in lid-margin scrapings than in scrapings from infected scalps.

5. Animal and human inoculations with cultures of P. ovale, or with lid margin scrapings from seborrheic blepharitis, produced temporary inflammations from which the organism could be isolated, but failed to reproduce the clinical signs of seborrheic dermatitis.

6. Intradermal injections of P. ovale extract in 16 individuals without gross seborrheic blepharitis or dermatitis of the scalp produced questionable or negative reactions; in 5 of 46 individuals with seborrheic dermatitis of the eyelids, on the other hand, the injections produced significant skin reactions. Three of the five showed severe conjunctival and corneal lesions. This suggests the possibility that sensitization may be a factor, particularly in the production of corneal lesions.

7. The present study provided no conclusive evidence that P. ovale was pathogenic for the eye and its adnexa but the following findings were suggestive of an etiologic relationship; (1) The constant occurrence of the organism in the lesions; (2) the apparent relationship between the number of organisms present in scrapings and the severity of the clinical disease; (3) the absence of the organism, or its exceptional presence in small numbers only, in clinically normal eyes; (4) the inability of the organism, unlike most saprophytes, to grow on any but complex media; and (5) the demonstration, by intradermal skin tests, of sensitization to the organism.

524 Sainte Claire Building,
San Jose, California.

References

[1] Malassez, R. Arch. de Physiologie, 1874, v. 1, series 2, p. 451. Cited from Benham.[4]
[2] Kile, R. L., and Engman, M. F. Further studies of the relation of Pityrosporum ovale to seborrheic eczema. Arch. Derm. & Syph., 1938, v. 37, p. 616.
[3] Thygeson, P. Etiology and treatment of blepharitis. Arch. of Ophth., 1946, v. 36, p. 445.
[4] Benham, R. W. The cultural characteristics of Pityrosporum ovale—a lipophilic fungus. J. Investigative Derm., 1939, v. 2, p. 187.
[5] ———. Pityrosporum ovale—a lipophilic fungus. Thiamin and oxalacetic acid as growth factors. Proc. Soc. Exp. Biol. and Med., 1945, v. 58, p. 199.
[6] Moore, M., Kile, R. L., Engman, M. F., Jr., and Engman, M. F. Pityrosporum ovale. Cultivation and possible role in seborrheic dermatitis. Arch. Derm. & Syph., 1936, v. 33, p. 457.
[7] Sulzberger, Marion B. Dermatologic Allergy. 1940, Springfield, Ill., Charles C Thomas, p. 259.

CONJUNCTIVITIS WITH MEMBRANE FORMATION*

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It is intended to present: (1) A classification of cases of conjunctivitis which develop membranes; (2) the pathogenesis of membrane formation which accompanies conjunctivitis; (3) case reports of typical examples of membranous conjunctivitis; (4) studies on the pathogenicity of corynebacteria recovered from diseased conjunctivas.

I. CLASSIFICATION OF CONJUNCTIVITIS EXHIBITING MEMBRANES

1. Bacterial
   a. Acute diphtheritic
      Acute streptococcic
      Acute pneumococcic
      Acute meningococcic
      Acute gonococcic
      Acute Koch-Weeks
      Acute Bacillus coli
      Acute B. faecalis alcaligenes
      Acute B. dysenteriae
      Acute Vincent's
   b. Chronic streptococcic
      Chronic tuberculous
2. Due to viruses
      Acute herpes febrilis
      Acute epidemic keratoconjunctivitis
      Acute vaccinial
      Acute inclusion blennorrhea
3. Due to higher plant parasites
      Chronic thrush
      Chronic streptothrix
4. Toxic
      Acute—in erythema multiforme
      Acute—in pemphigus
5. Allergic
      Acute (transient)—in vernal catarrh
6. Traumatic
7. Chemical
8. Due to unknown or uncertain causes
      Chronic ligneous

II. PATHOGENESIS OF MEMBRANE FORMATION ON THE CONJUNCTIVA

Membrane formation on the conjunctiva may result from a variety of local infectious, allergic, or traumatic lesions. At times it occurs in conjunction with constitutional diseases, or becomes apparent as a result of a general toxemia. Considerable investigative work has been performed to elucidate the nature of membrane formation.[1-6] It is now well known that the conjunctiva reacts to injuries with the frequent production of membranous lesions. The membrane formation is characteristic in some diseases. This mucosal reaction depends upon the tissue itself, and the duration of action, and concentration of the causative agent. There is ample evidence that the membrane which accompanies infectious diseases is formed exactly as the membrane which follows chemical injuries.[2] Some agents which are fairly toxic at first produce a light membrane; if their action continues an adherent membrane is formed. Occasional bacteria, such as the diphtheria bacillus, may produce either a catarrhal,[3, 7, 8] pseudomembranous, or membranous conjunctivitis.

The objective appearance of membranes has caused them to be classified into two main groups: (1) Pseudomembranes, and (2) true membranes.

Pseudomembranes are produced by the coagulation of a fibrinous exudate on the inner surface of the conjunctival epithe-

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lum. Numerous leukocytes, red blood cells, and desquamating epithelial cells are found enmeshed in the fibrin. There is no close connection between this coagulated fibrin and the underlying tissues, so it is easily removed. It should be emphasized that in some diseases, such as inclusion blennorrhea and vernal catarrh these pseudomembranes are frequently transient in duration and seldom recur. At other times, they are more permanent, tend to recur soon after removal, and persist until the toxic agent has been overcome by the tissues. Still others may be of long duration, recurrent in type, and resistant to therapy.

True membranous conjunctivitis is characterized by a massive exudation of fibrin and albuminous fluid into the epithelium and superficial substantia propria. This exudate is also coagulated on the inner surface of the epithelium. In those cases following a milder course, this persists and the membrane undergoes lysis or may be removed with complete healing. More severe cases are characterized by necrosis and the whole membrane may be sloughed off, leaving a raw bleeding surface. The surface may again become covered with a membrane. As the tissues overcome the infection, the membrane ceases to form and new epithelium covers the raw surface. In the most severe cases, toxins or chemicals may produce widespread vascular damage with thrombosis. As a result, considerable sloughing of the conjunctiva may occur with subsequent formation of adhesions between the lids and globe.

III. Case reports and discussion of the various groups of conjunctivitis

1. Bacterial membranous conjunctivitis

a. Diphtheritic conjunctivitis

Diphtheritic conjunctivitis may occur as: (1) An acute catarrhal conjunctivitis, (2) a pseudomembranous conjunctivitis, and (3) a true membranous conjunctivitis. Sourdille[3] first established the existence of the catarrhal form of diphtheritic conjunctivitis. This form responds readily to treatment with antitoxin. Sourdille[2,3] and Stephenson[6] have described a moderately acute form of diphtheritic conjunctivitis which is accompanied by pseudomembrane formation. This type is more severe than the catarrhal form. The symptoms usually subside following administration of diphtheria antitoxin. Most cases of diphtheritic conjunctivitis are accompanied by true membrane formation. Stephenson found membranes in 42 of 43 cases. Of these, 20 cases had a mild form of the disease, 19 were moderately severe, and 3 were severe. He stated that in most instances the patients showed pseudomembranes. The grave form of the disease is nearly always accompanied by true membrane formation, conjunctival necrosis, and sloughing. Corneal complications are frequent in this type of diphtheritic conjunctivitis.

Case report. *Acute diphtheritic membranous conjunctivitis.* Dr. H. C. I., aged 38 years, was admitted to the Institute of Ophthalmology, Presbyterian Hospital, April 4, 1941.

History. The patient awakened one morning with redness and watering of both eyes. He treated himself with zinc-sulfate drops for two days without improvement. He then shifted to mercurochrome (1 percent) for two days without effect. At this time local treatments with silver nitrate were commenced and within a few days he accidentally received a drop of 10-percent, instead of ½-percent, silver nitrate in each eye, which put him in bed for about a week. At the end of this time, conjunctival cultures showed only staphylococcus albus. He treated himself again for another week with mercurochrome but the membranes which had

developed failed to disappear.

Examination. There was a bilateral acute catarrhal conjunctivitis with membrane formation on the lower tarsal conjunctiva (fig. 1). The cornea was normal. Smears revealed numerous organisms having the morphology of C. diphtheria. Cultures showed a fair number of colonies possessing the characteristics of C. diphtheria. Subsequently, these organisms proved to be C. diphtheria by culture and guinea-pig inoculation.

Treatment. He was treated with diphtheria antitoxin intramuscularly and made an uneventful recovery.

Comment. This case presents a typical instance of chronic diphtheritic membranous conjunctivitis, persisting in spite of the ordinary forms of treatment but responding readily to diphtheria antitoxin.

Diagnosis. The diagnosis in acute diphtheritic conjunctivitis should be based upon the finding of typical organisms in smears and in cultures upon Loeffler's media. The virulence of these organisms must be confirmed by intraperitoneal inoculation of guinea pigs.

b. Acute streptococcic membranous conjunctivitis

Streptococcic membranous conjunctivitis may be accompanied by formation of either pseudomembranes or true membranes. The membranes which are encountered in moderate forms of the disease are usually pseudomembranous in type and are either transient or persistent. In these, the membrane appears during the second or third day of the disease, may be diffuse or localized, and principally affects the palpebral conjunctival. The bulbar conjunctiva and cornea are rarely involved. The membranes persist for the duration of the acute infection.

Other cases[9] are characterized by an acute fulminating conjunctivitis, edema of the lids, preauricular lymphadenopathy, diffuse palpebral and bulbar membrane formation, early corneal involvement with perforation, and a profuse conjunctival discharge. A number of cases[10–13] of chronic streptococcic conjunctivitis have been reported in which the infection was characterized by a brawny induration of the eyelids, extensive heavy membrane formation on the palpebral and bulbar conjunctiva, secondary corneal involvement with perforation, and a strong tendency to form layers of connective tissue in the substantia propria of the conjunctiva. In most of the cases of this type the infection has persisted for 1½ to 8 years. The prognosis is poor as to vision but the conjunctival lesions seem to have been favorably influenced by penicillin, sulfonamides, and antistreptococcic serum.

Fig. 1 (Hogan). Diphtheritic membrane on tarsal conjunctiva.

CASE REPORT. *Acute streptococcic membranous conjunctivitis with corneal perforation.* V. C., a Negro girl, aged seven years, was first seen at the clinic of the Institute of Ophthalmology, Presbyterian Hospital in New York, on November 16, 1942.

History. The patient had an upper respiratory infection which commenced approximately on November 6, 1942. On November 11th, the right eye became inflamed and swollen and developed a yellowish purulent discharge. On the

following day, the left eye became involved in a similar manner. The swelling and discharge increased in amount each day until she was referred to the hospital for care.

Examination. There was marked edema of the lids of both eyes (fig. 2). They could be separated only with difficulty. The bulbar conjunctiva was markedly

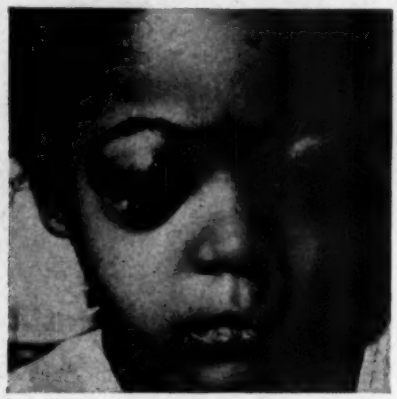

Fig. 2 (Hogan). Bilateral streptococcic membranous conjunctivitis.

chemotic. There was a good deal of yellowish discharge. A yellow-white membrane covered the palpebral and bulbar conjunctiva and extended across the cornea. The membrane was heavy and could be lifted only with difficulty, leaving a raw bleeding surface.

Course. The patient was admitted to the Hospital. Smears and cultures on blood agar were taken, and sulfadiazine and sulfanilamide were given by mouth and by local instillation in solution. On the following day the patient was extremely toxic. The blood sulfanilamide level was 15 mg. percent, and the blood sulfadiazine level was 6 mg. percent. The cornea of the right eye ruptured during the afternoon of this day. The left cornea soon showed signs of advanced necrosis and perforated. Subsequent therapy gradually brought the conjunctival infection under control. By January 10, 1942, the membranes had disappeared and the eyes showed beginning atrophy with extensively scarred granulating corneas.

Laboratory studies. The initial cultures on admission showed a pure culture of beta hemolytic streptococcus on both conjunctivas. Smears showed organisms which were morphologically similar to streptococci. In spite of continuous treatment, the smears and cultures from the membranes and corneas continued to be positive until January 8, 1942. The streptococci recovered from all of these cultures were reported to be in Group A, Type 25 (Lancefield). Subsequent cultures showed only occasional staphylococci and numerous diphtheroids.

Organisms from cultures on blood-agar plates were inoculated into the right cornea of a rabbit by the scratch method and into the left cornea by a penetrating needle. The right cornea developed a gray, 4-mm. nebula which cleared rather quickly. The left cornea developed a severe keratitis with necrosis superiorly and marked bulbar congestion. The infection subsequently subsided with formation of leukomas.

Comment. This case of acute streptococcic membranous conjunctivitis demonstrates the rapidity with which streptococci can invade the tissues, produce a severe inflammatory reaction, and result in corneal necrosis. The membrane formation in this case was in the nature of a true membrane. Streptococcic infections respond to penicillin and the sulfonamide compounds. Those patients treated early should rarely develop corneal complications. Swan and Allen[14] have reported favorably on the use of sulfanilamide in streptococcic membranous conjunctivitis.

c. Acute membranous conjunctivitis due to other bacteria

The membranous conjunctivitis which occurs during the course of pneumococcic, Koch-Weeks, influenza bacillus, gonococcic, and intestinal bacillary infections is usually of the pseudomembran-

ous form. In some instances, the pseudomembrane is permanent and subsides only with healing of the conjunctivitis. In others, such as gonorrheal infections, the membrane is usually transient in character. Gifford[15] stated that the pseudomembrane in pneumococcic infections was usually light and could easily be wiped off the upper tarsus. Morax[16] described four cases of pneumococcic conjunctivitis in children which were uniocular and accompanied by thin membranes. Clinically, the membranous conjunctivitis is identical in pneumococcic, influenza bacillus, and Koch-Weeks bacillus infections, and can be differentiated, as a rule, only by laboratory study. Knapp[17] reported a six weeks' old infant with inflamed eyes and fibrinous membranes on the upper lids. The child developed right corneal involvement 12 days after onset of the disease. He was able to culture the influenza bacillus on blood-agar plates, from material removed from the conjunctiva. Yakovleva[18] has reported a family epidemic of acute catarrhal conjunctivitis due to B. faecalis alcaligenes and B. dysentery liquefaciens. Five cases of the disease developed and of these a 2½-year-old girl had a thick membrane which was difficult to remove. She also had thickened, heavy lids and a profuse purulent discharge.

Comment. The diagnosis in these acute forms of conjunctivitis with membrane formation is usually made by examining stained smears of the conjunctival exudates and by the culturing of the causative organisms on suitable media.

Treatment. It is best to direct treatment toward eliminating the causative organism and providing palliation of the patient's symptoms. The pneumococcus and gonococcus respond to sulfonamides and penicillin administered locally and systemically. Koch-Weeks and influenza bacillus infections usually respond to mild antiseptics and are self-limiting infections. There is a possibility that conjunctivitis due to intestinal bacteria may be relieved by local streptomycin therapy.

d. Chronic tuberculous membranous conjunctivitis

Most cases of conjunctival tuburculosis are characterized by either ulcerative or nodular lesions. Gourfein[19] reported the case of a six-year-old girl with swelling, redness, and discharge from the right eye. On examination, the upper tarsal conjunctiva was covered with a gray false membrane. It detached with difficulty and resulted in bleeding but there was no underlying ulcer. There was a right preauricular, submaxillary, and parotid lymphadenopathy. Chest examination was negative. The lesion was completely healed in 21 days without complication. Cultures showed only the staphylococcus albus. Guinea pigs were inoculated with bits of the false membrane and died four months later of generalized tuberculosis. The purulent exudate from several glands was also injected subcutaneously into guinea pigs and they died three months later of generalized tuberculosis. Conjunctival secretion was injected into the anterior chamber of guinea pigs with formation of tubercles on the iris and subsequent death of the animals from generalized tuberculosis.

Comment. The course of the disease in the above case is somewhat atypical, and the author does not say whether or not he observed tubercle bacilli in smears from the conjunctiva. However, the animal inoculations in this case are rather convincing, and it must be presumed that the case is actually one of chronic tuberculous membranous conjunctivitis.

2. MEMBRANOUS CONJUNCTIVITIS DUE TO VIRUSES

a. Inclusion blennorrhea

During the acute phase of inclusion blennorrhea a pseudomembrane may form on the palpebral conjunctiva both inferi-

Fig. 3 (Hogan). Pseudomembrane in epidemic keratoconjunctivitis.

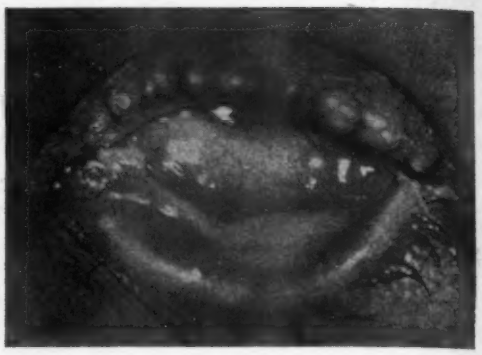

Fig. 5 (Hogan). Membrane in epidemic keratoconjunctivitis.

orly and superiorly. This membrane is temporary and usually disappears within 10 days to 2 weeks. The membrane, at times, may be quite transient. Thygeson[20] has pointed out that no sequelae are noted except that marked pseudomembranous infections may be followed by fine conjunctival scars.

b. Epidemic keratoconjunctivitis

Membrane formation in epidemic keratoconjunctivitis was first reported in 1942 by Hogan and Crawford.[21] Of their 125 reported cases, 17 patients developed membranes on the conjunctiva of the eyelids.

CASE REPORTS. These 17 patients were seen in the fall of 1941. They all had typical cases of epidemic keratoconjunctivitis and exhibited conjunctival membranes. The membrane made its appearance in each of these patients between the 4th and 8th days after onset of the disease. At first it was thin and milky in appearance and was usually located on the tarsal conjunctiva near the fornix. It could be wiped off easily. In three cases, the membrane persisted in this form for several days and then disappeared (fig. 3). In the other 14 cases, the membrane continued to form and extended medially onto the caruncle and semilunar fold and toward the margin of the lids. In two instances, a thin pseudomembrane occurred on the bulbar conjunctiva inferiorly (fig. 4). As the membrane developed it became more dense and white and in four cases was difficult to remove (figs. 5 and 6). Moderate bleeding occurred after removal. The membrane in these more severe cases usually lasted from 6 to 8

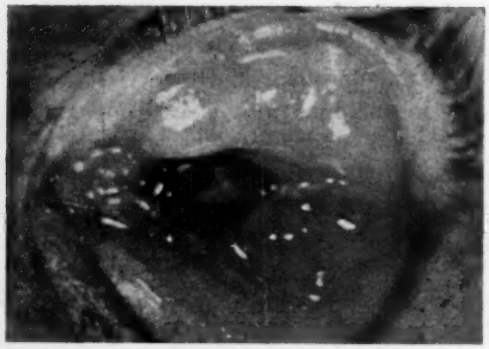

Fig. 4 (Hogan). Thin membrane in epidemic keratoconjunctivitis.

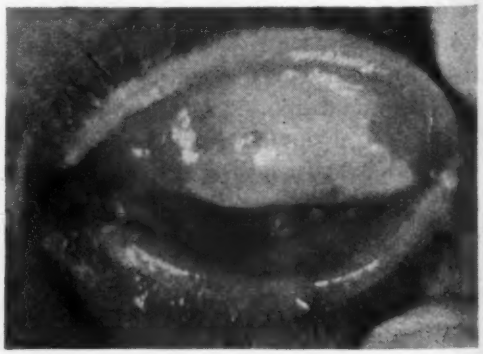

Fig. 6 (Hogan). Membrane in epidemic keratoconjunctivitis.

days. After subsidence of the infection, no scars were noted on the conjunctiva.

Sporadic cases of epidemic keratoconjunctivitis have been seen since 1942, but no instances of membrane formation have occurred until this year. The membrane, in the more recent cases, is thin in appearance and more transient in duration. In addition, we have also noted atypical forms of the disease. Recently a physician was seen who developed a bilateral acute catarrhal conjunctivitis, more severe in the right eye. There was a pseudomembrane on the tarsal conjunctiva of the right eye but none on the left, and there was no preauricular lymphadenopathy. There were fine scattered epithelial corneal infiltrates in both eyes. Laboratory studies showed organisms resembling C. diphtheria in smears, but repeated cultures showed only diphtheroids, nonpathogenic to guinea pigs. The patient was treated with diphtheria antitoxin, 40,000 units being given on two occasions. He showed steady improvement and the conjunctivitis was cured within 10 days. He had been treated with penicillin before coming for advice, so that if his infection was originally diphtheritic the organisms were probably gone by the time the above studies were made. At present, this patient shows corneal opacities which are exactly similar to those of epidemic keratoconjunctivitis. The wife of this patient also developed a conjunctivitis but without membrane formation. Her infection was accompanied by epithelial lesions which resembled those of a herpetic keratitis. Laboratory studies on this patient were negative. Five patients of the above physician also developed an acute conjunctivitis during the course of his infection. In these patients a keratitis developed which had the features of a dendritic keratitis.

Comment. The clinical features of epidemic keratoconjunctivitis, together with the laboratory findings, especially the observation of a predominantly lymphocytic exudate in scrapings, serve to distinguish this disease from most others with membranous conjunctivitis. Treatment in these cases, so far, is of little value except that palliative measures may render the patient more comfortable. Convalescent serum may eventually prove to be of value, especially if given in the early stages of the disease.

c. Herpes febrilis

Clausen,[22, 23] Aust,[24] and Batagnani[25] have shown that a catarrhal form of conjunctivitis may occur in herpes febrilis, especially if the patient has lesions on the lid margins. Aust, Loewenstein,[26] Granström,[27] and Larsson and Granström,[28] have reported cases of acute conjunctivitis associated with marginal lid lesions, membrane formation, severe pain, regional lymphadenopathy, and constitutional symptoms. A number of these patients subsequently developed dendritic keratitis or exhibited superficial epithelial corneal infiltrates. Rabbit corneal inoculations with scrapings from these cases were accompanied by development of a keratitis, conjunctivitis, iritis, and, at times, cerebral symptoms. Loewenstein thinks that the infections in these cases originate on the lid margins and result in pseudomembranous conjunctivitis with corneal lesions. Granström and Larsson think the herpes virus must be suspected as a cause of violent cases of unilateral conjunctivitis in which a bacterial factor cannot be proved. They conclude that the development of keratitis, enlarged lymph nodes, membrane formation, and positive rabbit inoculations confirm the diagnosis.

d. Vaccinia

Many reports have been made concerning the development of conjunctivitis and corneal ulcers during the course of smallpox. A number of articles state that the streptococcus is frequently cultured from

the conjunctiva in cases showing the eye complications of smallpox. It is probable that the conjunctival pustules become secondarily infected in many instances, with development of severe ulceration and membrane formation. Almost 100 cases of accidental vaccination of the conjunctiva have been reported. Most of the reported cases have developed the conjunctival lesion as a result of contact with the vaccinia vesicle on other persons (case 2, below).

CASE REPORT. (1) In 1946 a patient was seen who developed an accidental vaccinia of the eyelids accompanied by a membranous conjunctivitis. The patient, a woman, aged 35 years, had been vaccinated on the right arm eight days prior to coming for treatment. She had noted swelling of her right eyelids for three days, with redness and moderate discharge from the conjunctiva.

Examination. There was marked edema and redness of the lids. The conjunctiva was edematous and congested. There was a thin, pale, white, pseudomembrane on the lower tarsal conjunctiva and fornix. The cornea was normal. There was a small nodule topped by several vesicles on the upper lid temporally. A vaccinia pustule was present on the right arm.

Course. The conjunctivitis subsided slowly and the pseudomembrane disappeared from the conjunctiva in five days, without scarring.

CASE REPORT (2). I am indebted to Dr. Margaret Henry for permission to present the findings in this patient. A Negro girl, aged six years, was admitted to the Children's Hospital on April 17, 1946, with the history that three days previously the left lower lid had become swollen. Within 24 hours she could not open her eye. Skin lesions soon appeared on the eyelids and bridge of her nose. Her physician administered 20,000 units of diphtheria antitoxin the following day and referred the patient to the Hospital.

Examination. The appearance of the left eye was striking. There was marked periorbital edema and cellulitis, extending above the eyebrow, across the nose, and down onto the cheek. There was a watery discharge from the eye, and the lids were covered with a dry purulent exudate. There were several small vesicles on the eyelid and one umbilicated vesicle on the bridge of the nose. There were also a number of vesicles on the lid edges. On retracting the lids, there was a thin pseudomembrane on the lower tarsal conjunctiva near the lid margin and on the upper tarsus centrally.

Course and Treatment. The patient was given another 20,000 units of diphtheria antitoxin intramuscularly. Four days later she was afebrile, and the conjunctival and lid lesions were nearly well. The lesion on the bridge of the nose looked like a primary vaccinia. Five days later the patient developed a small, pinhead-sized ulcer at the 6-o'clock position on the cornea which healed rapidly under treatment with tincture of iodine. She was discharged on April 28th.

Laboratory findings. Repeated cultures and smears of the conjunctiva showed no pathogenic organisms. Throat cultures showed no diphtheria bacilli. The Kahn test was negative.

Comment. There is some debate as to the etiology of this condition, as the child had no history of vaccination. However, she had been playing with cousins who had active vaccinia lesions and she may have contracted the virus from them. She was vaccinated twice while in the Hospital and showed an immune reaction. The clinical appearance of the lesion on the bridge of the nose was rather typical, so that a diagnosis of vaccinia membranous conjunctivitis was made in this case. The experiments of Folk and Taube[29] provide ample evidence that vaccinia virus, intro-

duced on the conjunctiva, is well able to produce a membranous conjunctivitis without a previous abrasion. In spite of the severity of the clinical picture in these cases the prognosis is surprisingly good, and most reports indicate that the lesions heal without visual loss in about 90 percent of the cases.

3. Membranous conjunctivitis due to higher plant parasites

At times, a conjunctivitis may develop in patients suffering from general debilitating diseases. Cases have been reported in which smears showed fungi or other parasites. Usually other organisms have been encountered in addition to the fungi, and the decision as to the nature of the causative agent is difficult. Most fungus infections of the conjunctiva are granulomatous in form, and rarely become diffuse with membrane formation. Several case reports have been made describing membranes on the conjunctiva due to Oidium albicans and the streptothrix.

a. Thrush

Norton[30] reported the case of a five-year-old boy who exhibited symmetrically placed white growths nasally and temporally outside the limbus in the palpebral fissures. The outer lesions were triangular in shape and the inner ones were smaller and quadrilateral. This case was followed for a month, and the lesions recurred quickly after removal. The conjunctiva beneath the lesions was wrinkled, yellowish, and slightly chemotic. Otherwise, the conjunctiva was normal, and the boy had no symptoms. Smears and cultures showed monilia candida with mycelium and spores. A sister of this boy was said to have the same condition.

Pichler[31] reported two cases. The first was of a four months' old child having a severe pseudomembranous conjunctivitis and an aphthous stomatitis. The child's nurse was similarly affected orally. Oidum albicans was found on the membranes. The second case, that of a three-year-old girl with several exanthematous diseases, showed general emaciation and acute conjunctivitis. There was a white dry membrane on the tarsal and bulbar conjunctivas and the corneas. Similar lesions occurred in the mouth and nose. The conjunctival and corneal lesions resulted in scarring and opacification. Oidium albicans was found in smears from the conjunctival and oral lesions, but cultures were unsuccessful.

b. Streptothrix

May[32] reported a patient with conjunctivitis accompanied by a firmly adherent thin, yellow-white membrane. The bulbar conjunctiva was red and thickened. There was an ulcer below the limbus measuring a quarter of an inch in diameter. It was covered by a thin membrane. Smears and cultures were negative, but tissue sections showed the streptothrix.

4. Membranous conjunctivitis caused by toxic agents

a. Erythema multiforme

The first case of erythema multiforme associated with conjunctival lesions was reported by Fuchs,[33] in 1876. Since that time, a large number of cases have been reported.[34–38]

In general, two conjunctival forms of the disease are seen: (1) A mild simple catarrhal conjunctivitis, and (2) a severe membranous conjunctivitis. The onset in most cases is similar to an acute infectious disease with chills, fever, headache, and malaise. The skin lesions are widespread and polymorphous in character. Conjunctivitis, rhinitis, stomatitis, and pharyngitis are frequently seen.

The ocular lesions usually consist of an intense pseudomembranous inflammation of the conjunctiva and corneal epithelium. The prognosis, from an eye standpoint, is frequently unfavorable. Raffin[39] has

stated that the lesions are primarily inflammatory, soon become covered with fibrin, and appear as pseudomembranes. Ulceration is not uncommon and symblepharon may occur. Corneal involvement occurs all too frequently. It commences with edema of the epithelium and stroma. Membrane formation follows and leads to ulceration and perforation. Healing always occurs, with a certain amount of atrophy and scarring.

Erythema multiforme is usually due to sensitivity to drugs or sera. Spontaneous cases may occur in young people and in them the causative agent is rarely determined. Most people are agreed that the disease is toxic in origin.

Two cases have been seen during the past few years which have presented the features of erythema multiforme accompanied by mucous membrane involvement. I am indebted to Dr. David O. Harrington and Dr. Margaret Henry for permission to present them.

CASE REPORT (1). A. K., a white man, aged 35 years, was admitted to the United States Veterans Hospital in San Francisco on September 29, 1946, for treatment of cerebral concussion and a compound fracture of the skull. During the course of his treatment he received 30,000 units of penicillin intramuscularly every four hours and 1 gm. of sulfadiazine by mouth every four hours. This was continued for 18 days, at which time he developed a severe generalized dermatitis, characteristic of erythema multiforme. The conjunctival and oral mucous membranes were markedly affected and he had a temperature of 104°F. In spite of the high degree of fever, his white blood count remained at around 5,000 cells per cubic ml., with a normal differential count.

Eye examination. The lids and conjunctivas were markedly chemotic, with a thick tenacious mucoid discharge. A thin pseudomembrane covered the lid and bulbar conjunctivas. Treatment was symptomatic and improvement was slow. Ulcers formed beneath the pseudomembranes, and there was a marked tendency to form a symblepharon. Attempts to separate the membranes left raw bleeding areas. At first there was no corneal involvement, but as the disease progressed, a gray haze was seen superficially. At the end of 15 days, the cornea was clear and membrane formation ceased. Subsequently it was noted that there were two quite firm adherent symblepharons in the upper and lower fornices of both eyes. There was no limitation of motion of the globes. Visual acuity was normal.

CASE REPORT (2). Mrs. K. A., aged 28 years, was first seen at Children's Hospital on October 10, 1944, complaining of a skin eruption with pruritus, headache, sore throat, and swollen eyes and lips for 48 hours.

History. The patient had been perfectly well until 48 hours before admission, when she noted the signs of an upper respiratory infection, including headache, malaise, a nasal discharge, backache, pains in her legs, and sore throat. Twenty-four hours later a conjunctivitis developed in both eyes, and later the same day puffiness of the lips. She had extreme difficulty in swallowing. Six to eight hours prior to onset of the conjunctivitis she had taken an aspirin preparation containing phenolphthalein. Twelve hours before admission her physician commenced sulfathiazole (2 gm.), followed by 1 gm. every four hours. On the morning of admission the patient developed a scattered rash on the skin. Her family and past medical histories gave no indication of a cause of the present illness.

Examination. The patient was acutely ill. There was a generalized eruption of the face, trunk, and extremities, including the palms of her hands and soles of her feet. The mucous membranes of the eyes were edematous and injected; the mouth

showed a peculiar purplish-yellow discoloration.

Eye examination. The eyes were swollen shut and there was an acute bilateral conjunctivitis with severe photophobia and a serous discharge. The corneas and intraocular structures appeared normal.

Course. The skin and mucous membrane lesions remained very much the same until October 18, 1944 (one week later), at which time the patient complained of inability to see from the left eye. On examination there appeared a rather extensive pale-yellow gelatinous membrane on the conjunctiva of the right eye. A similar membrane on the left eye completely covered the bulbar conjunctiva and the cornea. The membrane over the cornea was lifted up by a serous exudate and air, forming a very extensive bulla. Cultures were taken at this time, and it was seen that the membrane over the left cornea was easily removed with the applicator. The underlying cornea appeared normal. Two days later the corneal membrane was gone in the left eye, but that on the palpebral conjunctiva remained. On October 25, 1944, the conjunctivitis was practically well and there was no secretion. A few white linear scars could be seen on the upper palpebral conjunctiva. The corneas appeared normal. By October 30, 1944, the skin lesions had practically disappeared. The condition of the lips and mouth was still bad, although healing. She was discharged to the care of her family physician at this time.

Comment. These two cases illustrate the development of erythema multiforme accompanied by mucous-membrane lesions as a result of the toxicity of drugs. The course of the disease in both cases was unusually favorable, inasmuch as the corneas were not damaged. The membrane which forms in erythema multiforme is more of the nature of a true membrane, as necrosis of the conjunctiva occurs and scarring may result. Treatment in cases of this type must be directed along general lines to eliminate the toxic agent. Local therapy should be aimed at preventing corneal complications and symblepharon.

b. Pemphigus

Pemphigus is a toxic disease which may affect the eyes in both the acute and chronic forms. In those cases which present a vesicular eruption on the conjunctiva, the vesicles not infrequently rupture and the fibrinous fluid coagulates to form thin localized membranes. Diffuse membrane formation is not characteristic of pemphigus, but local pseudomembranes may form in the areas of ruptured vesicular lesions.

5. ALLERGIC MEMBRANOUS CONJUNCTIVITIS

a. Vernal catarrh

Thin transient membranes may form on the conjunctiva of the tarsus at any time during the acute phase of vernal catarrh. These transient membranes seem to depend upon the coagulation of a fine film of fibrin on the inner surface of the epithelium. Herbert[40] mentions that, if the lids are held everted for a short while, a fine membrane may be produced, and that if an examination is made at this time, eosinophils can be found. Lehrfeld[41, 42] distinguishes the milky film which has been described in vernal catarrh and which is due to the subepithelial hyaline degeneration, from the thick, ropy, lardaceous film which occurs on the mucous membrane in this disease. He states that this tenacious fibrinous membrane is somewhat elastic and can be wiped off without bleeding.

6. MEMBRANOUS CONJUNCTIVITIS DUE TO CHEMICALS

That a membranous conjunctivitis may be produced by chemicals has been shown by numerous observers.[2, 43] Most of the

original work on the pathology of membrane formation was done following chemical production of the membranes. Jequirity, lime, ammonia, and silver nitrate are the drugs most frequently mentioned as producing membranes. Arsenic administered parenterally may produce a toxic reaction with exfoliative dermatitis and mucous-membrane lesions. Hegner[44] mentions a patient who received neoarsphenamine and developed an exfoliative dermatitis. A pseudomembranous conjunctivitis occurred, followed by corneal necrosis and panophthalmitis.

The development of membranes on the conjunctiva, following chemical injury, depends upon the ability of the drug to penetrate the epithelium, upon its concentration, and duration of action.

7. Membranous conjunctivitis due to unknown or uncertain causes

A fairly large number of cases of chronic membranous conjunctivitis have been reported under a variety of titles. In a number of these,[45-49] bacteriologic studies revealed organisms, such as staphylococci, streptococci, and so forth. It is probable that most of these chronic membranous conjunctivitis cases are streptococcic in origin.[13, 50] Among other cases which have been described, the membranes formed over ulcerated areas of the conjunctiva and were followed by granulomatous overgrowths. Later organization of these granulomas led to the formation of dense masses of connective tissue resembling hyaline.

Future cases of this type will probably be classified among the above described groups of bacterial conjunctivitis.

IV. Studies of the pathogenicity of diphtheroids

In connection with diphtheritic membranous conjunctivitis, an attempt was made to determine if pathogenicity could be induced in any of the diphtheroids recovered from the conjunctiva. The diphtheroid organisms are generally considered to be saprophytic; and the organisms on the conjunctiva have never been thought to become pathogenic.[51] Numerous experiments designed to determine this pathogenicity have failed. On occasions pathogenic diphtheroids have been recovered in infections occurring in other portions of the body.[52-54]

There is evidence that some strains of diphtheroids, such as C. ovis[55] and C. ulcerans[56, 57] produce toxins and that some of these organisms are capable of causing human infections. Reference should be made to the case of chronic membranous conjunctivitis reported by Dunphy[58] in which organisms of the diphtheroid group were isolated.

Methods

Corynebacteria were recovered from the conjunctivas of 100 patients with a variety of conjunctival affections. These strains were obtained by implanting smears from the conjunctivas onto rabbit blood-agar plates. Colonies of diphtheroids were taken from the blood-agar plates and implanted in beef broth. After 24-hour incubation at 37°C., a loopful of the broth was spread on blood-agar plates. By further transplantation, pure cultures were then obtained in beef broth. The resulting 48-hour growth of the pure strain in this beef broth was used for morphologic studies, animal inoculations, and fermentation reactions.

The following animal studies were made:

a. Forty-eight-hour broth cultures of each strain were inoculated into the conjunctivas of mice, rabbits, and guinea pigs, one drop at a time at 10-minute intervals, for four hours.

b. One-tenth cc. of a 48-hour broth culture of each organism was injected

beneath the conjunctivas of guinea pigs, rabbits, and mice.

c. One-tenth cc. of a 48-hour broth culture of each organism was injected into the anterior chambers of rabbits and guinea pigs.

d. An equal portion of a 48-hour broth culture of each strain was mixed with an equal amount of *mucin*. Drops of this mixture were instilled into the conjunctival sacs of rabbits and of guinea pigs at 10-minute intervals for four hours.

e. Utilizing the same mixture as in (d) above, 0.1 cc. was injected into the anterior chamber and into the vitreous of mice, rabbits, and guinea pigs.

g. Diphtheria toxin was obtained diluted with saline so that it contained 450 m.l.d. per cc. This toxin was standardized so that upon instillation of one drop into a rabbit's conjunctival sac every 5 to 10 minutes for 2 to 2½ hours, a purulent conjunctivitis could be produced, which subsided within 2 to 4 days. This toxin was instilled into the conjunctival sac of rabbits every 10 minutes for two hours, followed each time by the instillation of a drop of a 48-hour broth culture of diphtheroid organisms. This procedure was carried out with the organisms derived from 10 different patients.

h. The toxin was instilled into the conjunctival sacs of rabbits and monkeys at 10-minute intervals for six doses. The conjunctival membrane was then lightly scrubbed with an applicator which had been dipped into a broth suspension of diphtheroids derived from five patients.

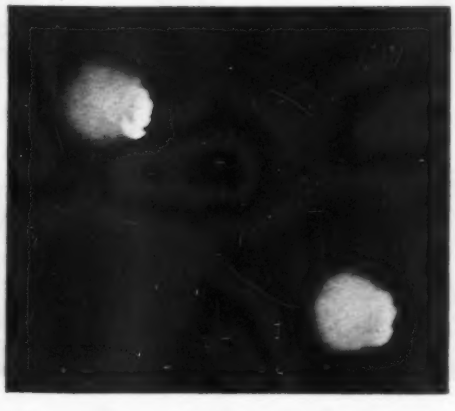

Fig. 7 (Hogan). Smaller granular diphtheroid colonies (Magnification ×10).

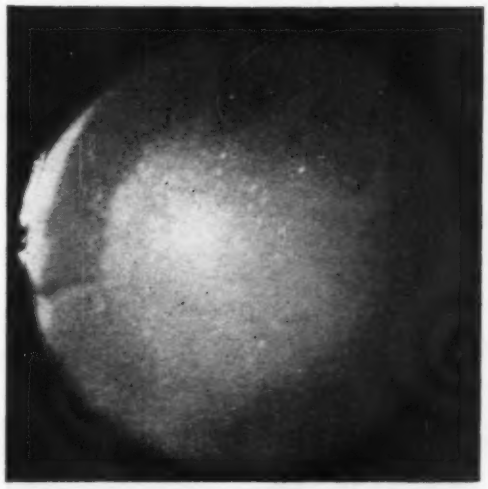

Fig. 8 (Hogan). Large granular colonies of diphtheroids (Magnification ×140).

Results

a. Colony morphology. The colony morphology was studied on 24-hour blood-agar cultures. Two main varieties of colonies were encountered in this study, the most frequent type being small, round, flat, and very slightly granular (fig. 7). The other type was larger, more elevated, round, and coarsely granular (fig. 8). This latter type might correspond with the previous descriptions of C. xerosis which was described as having a peculiar dryness or scaliness of growth on media.

b. Cellular morphology. Three main types of organisms were encountered in this series of cultures: (1) Slender, curved rods of varying length and an irregular staining protoplasm (fig. 9). (2) Small, thick rods, which stained either solidly or were barred and wedged (fig. 10). (3) Coccoid forms (figs. 11 and 12).

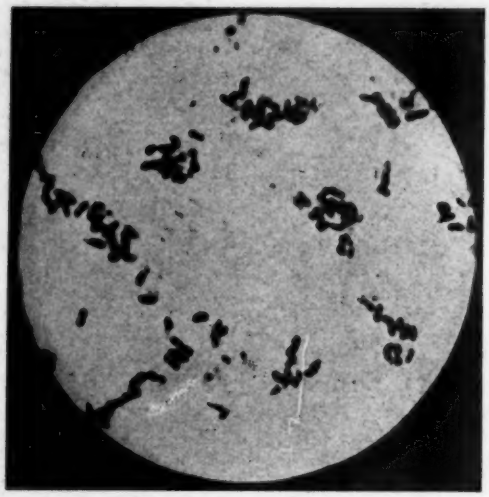

Fig. 9 (Hogan). Slender curved diphtheroids (Magnification ×1,200).

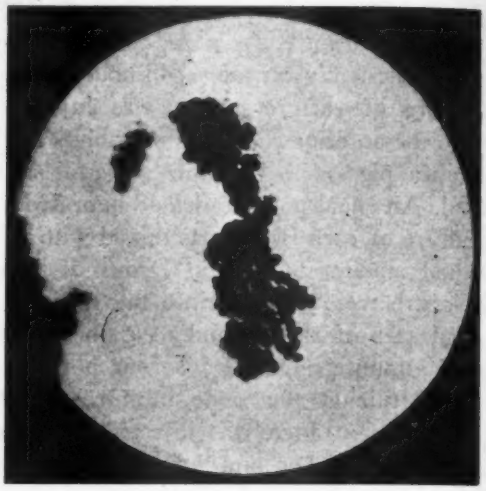

Fig. 11 (Hogan). Coccoid forms of diphtheroids (Magnification ×1,200).

The above descriptions apply to 24-hour cultures only. It is well known that after 24 hours, clubbing, irregular staining, elongation, and segmentation are more frequently encountered. No organisms were encountered which fulfilled the essential character of C. xerosis; and it is doubtful if C. xerosis is sufficiently characterized to deserve special mention in reports.

C. Hofmanni fits the description of the second organism (fig. 10), and the cultural characteristics bear out the presence of this organism on the conjunctiva.

c. Fermentation reactions. The tabulated results of fermentation reactions are recorded in Table 1.

Fig. 10 (Hogan). Short, thick, rodlike diphtheroids (Magnification × 1,200).

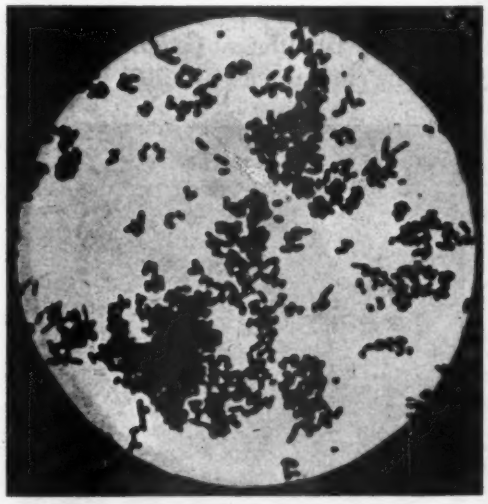

Fig. 12 (Hogan). Coccoid diphtheroids (Magnification ×1,200).

d. Animal experiments. In none of these experiments with the cultures of diphtheroids, alone or in conjunction with mucin, or with diphtheria toxin, was it possible to produce any ocular infections.

Comments

It is concluded from these experiments that diphtheroid organisms encountered on the conjunctiva during the course of infectious conditions probably play no part in the production of conjunctivitis and rarely, if ever, contribute to the production of intraocular infections. This work confirms previous experiments done on conjunctival diphtheroid organisms. The consideration arose, however, that these diphtheroid organisms might be rendered pathogenic if they could be protected by a substance such as mucin. Similarly, it was reasoned that the virulence might be developed if the resistance of the conjunctiva could be lowered by the use of diphtheria toxin alone or in conjunction with trauma. It was not found to be possible to alter the saprophytic nature of the organisms encountered. It was felt that occasional pathogenic diphtheroids might be encountered which might cause conjunctival disease, such as those described by Gilbert and Stewart and Reudiger.

None of the organisms encountered showed the characteristics of C. ulcerans or C. pyogenes. Cultures of C. ulcerans were obtained through the courtesy of Dr. Ruth Gilbert of the New York State Department of Health. These organisms invariably produced a rapid and destructive panophthalmitis when injected into the anterior chamber. It was noted that the effects of these injections could be minimized in guinea pigs and rabbits by the administration of diphtheria antitoxin. Unfortunately continued pursuance of this subject was interrupted by the war. Further studies will be made on the effect of C. ulcerans on the eye and its relationship to other ocular diphtheroids.

TABLE 1

CULTURAL CHARACTERISTICS OF 100 STRAINS DIPHTHEROID BACILLI

Colony Morphology		Bacterial Morphology			Positive Fermentation Reactions									
Granular	Smooth	Long Rods	Short Rods	Coccoid	Dextrose	Maltose	Galactose	Saccharose	Lactose	Dextrin	Mannitol	Indole	Nitrogen	Liquefied Gelatin
84	16	73	16	11	46	36	18	48	10	23	17	8	35	2

Conclusions

1. A classification of cases of conjunctivitis which develop membranes is presented.

2. The pathogenesis of membrane formation which accompanies various types of conjunctivitis is discussed.

3. The nature of the membrane formation among the various groups is discussed and case reports are given of typical examples in some of the groups.

4. Diphtheroids from 100 cases of external ocular disease were recovered in pure culture and studied for pathogenicity. No pathogenic organisms were encountered.

5. Attempts to enhance the pathogenicity of diphtheroids by utilizing the pro-

tective effect of mucin were unsuccessful.

6. Attempts to produce diphtheroid infections of the conjunctiva by lowering the resistance of the conjunctiva with diphtheria toxin and trauma were unsuccessful.

7. C. ulcerans, an organism recovered from the throat by Gilbert and Stewart produced a panophthalmitis on intraocular injection, but the effects could be minimized by previously administered diphtheria antitoxin.

Appreciation is expressed to Dr. Phillips Thygeson and Mrs. Clement McCulloch for valuable suggestions and assistance in carrying out the work of this paper.

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References

[1] Sourdille, Gilbert. Clinical studies, bacteriology and therapy of ocular diphtheria. Arch. d'Opht., 1893, v. 13, pp. 762-775.
[2] ———. False membranes of the conjunctiva; anatomy and pathologic physiology. Arch. d'Opht., 1894, v. 14, pp. 240-252.
[3] ———. Clinical studies, bacteriology and therapy of ocular diphtheria. Arch. d'Opht., 1894, v. 14, pp. 48-64.
[4] Coppez, H. Contribution to the historical study of pseudomembranous conjunctivitis. Arch. d'Opht., 1897, v. 17, pp. 314-327.
[5] Morax, V., and Elmassian, H. Action of diphtheria toxin in mucin membrane. Ann. de l'Inst. Pasteur, 1898, v. 12, pp. 210-225.
[6] Stephenson, Sydney. Membranous conjunctivitis. Trans. Ophth. Soc. Unit. King., 1902, v. 22, p. 59.
[7] Francois, J. Catarrhal diphtheritic conjunctivitis. Brit. Jour. Ophth., 1935, v. 19, Jan., pp. 1-19.
[8] Haas, E. Four cases of diphtheritic conjunctivitis without false membranes in subjects having diphtheria in nose and throat. Bull. et mem. Soc. franc. d'Ophth., 1936, v. 49, pp. 66-73.
[9] Rutherford, C. W. Membranous conjunctivitis with loss of eyeballs. Jour. Amer. Med. Asso., 1929, v. 93, pp. 1779-1784.
[10] Kalt, E., and Autier. Streptococcal pseudo-membranous conjunctivitis of prolonged duration. Bull. Soc. d'Opht. de Paris, 1927, v. 21, pp. 77-79.
[11] Vancea, P. Clinical considerations of some rare forms of grave streptococcic conjunctivitis. Arch. d'Opht., 1926, v. 43, Dec., pp. 724-731.
[12] Rutherford, C. W. Membranous conjunctivitis with persistent membrane completely covering the cornea. Trans. Amer. Ophth. Soc., 1933, v. 31, pp. 237-246.
[13] Kluever, H. C. Streptococcal pseudomembranous conjunctivitis. Report of a case. Amer. Jour. Ophth., 1935, v. 18, Dec., pp. 1094-1105.
[14] Swan, K. C., and Allen, J. H. Streptococcic pseudomembranous conjunctivitis treated with sulfanilamide. Amer. Jour. Ophth., 1939, v. 22, Nov., pp. 1255-1261.
[15] Gifford, H. The pneumococcus of Fraenkel as a frequent cause of acute catarrhal conjunctivitis. Arch. of Ophth., 1896, v. 25, pp. 314-324.
[16] Morax, V. Discussion of four cases of conjunctivitis in children due to pneumococcus uniocular with a thin membrane. These de Paris, 1894.
[17] Knapp, A. Severe pseudo-membranous conjunctivitis in an infant presumably due to the influenza bacillus. Arch. of Ophth., 1904, v. 33, pp. 386-388.
[18] Yakovleva, A. A. Familial epidemic of acute catarrhal and croupous conjunctivitis caused by intestinal bacteria. Sov. vestnik oftal., 1936, v. 9, pp. 354-355.
[19] Gourfein, D. Tubercular pseudo-membranous conjunctivitis. Arch. d'Opht., 1912, v. 32, p. 693.
[20] Thygeson, P. Inclusion blennorrhea. Personal communication, 1947.
[21] Hogan, M. J., and Crawford, J. W. Epidemic keratoconjunctivitis. Amer. Jour. Ophth., 1942, v. 25, Sept., pp. 1059-1078.
[22] Clausen, W. Herpes of the cornea with unusual manifestations. Klin. M. f. Augenh., 1927, v. 79, p. 839.
[23] ———. Discussion of paper on herpes of the cornea by Hentschel. Klin M. f. Augenh., 1933, v. 90, p. 548.
[24] Aust, O. Herpes febriles of the lid margins and the conjunctiva. Klin. M. f. Augenh., 1931, v. 86, p. 682.
[25] Batagnani, A. Conjunctivitis of the virus herpes in the newborn. Boll. d'Ocul., 1934, v. 13, Sept., pp. 1217-1220.

[24] Loewenstein, A. Occurrence of ulcers of eyelid, croupous conjunctivitis, angina, painful swellings of regional lymph nodes as clinical unit with herpes. Med. Klin., 1933, v. 29, Jan., pp. 9-11.
[25] Granström, K. O. Contribution to knowledge of importance of herpes infections in corneal and conjunctival affections, especially in membranous conjunctivitis. Acta Ophth., 1937, v. 15, pp. 361-369.
[26] Granström, K. O. and Larsson, S. A strange case of keratoconjunctivitis with the "Syndrome of Parinaud" transmissible to rabbits; (unilateral herpetic membranous conjunctivitis). Acta Ophth., 1931, v. 9, pp. 94-100.
[27] Folk, M. L., and Taube, E. L. Vaccinia of the eyelids and conjunctiva. Amer. Jour. Ophth., 1933, v. 16, Jan., pp. 36-39.
[28] Norton, A. H. Thrush of the conjunctiva, Amer. Jour. Ophth., 1927, v. 10, p. 357.
[29] Pichler, A. Thrush. Ztschr. f. Augenh., 1900, v. 3, p. 669.
[30] May, C. H. Streptothrix infections of the conjunctiva. In report of proceedings of the Section on Ophthalmology of the New York Academy of Medicine. Arch. of Ophth., 1917, v. 46, p. 171.
[31] Fuchs, E. Herpes iris of the conjunctiva, Klin. M. f. Augenh., 1876, v. 14, pp. 333-351.
[32] Stevens, A. M., and Johnson, F. C. A new eruptive fever associated with stomatitis and ophthalmia. Amer. Jour. Dis. Child., 1922, v. 24, Dec., pp. 526-533.
[33] Wheeler, J. M. Destructive purulent ophthalmia accompanying an eruptive fever with stomatitis. Amer. Jour. Ophth., 1930, v. 13, June, pp. 508-514.
[34] Benoit, Maurice. A case of non-diphtheritic pseudo-membranous conjunctivitis accompanied by bucco-pharyngeal eruptive lesions. Am. d'Ocul., 1935, v. 172, Mar., pp. 222-225.
[35] Barkan, H. Herpes iris of the conjunctiva, with report of a case. Arch. of Ophth., 1913, v. 42, pp. 236-240.
[36] Bailey, J. H. Lesions of the cornea and conjunctiva in erythema exudativum multiforme, (Hebra); report of three cases with grave ocular sequelae. Arch. of Ophth., 1931, v. 6, pp. 362-379.
[37] Raffin, A. Conjunctivitis, rhinitis and aphthous stomatitis with erythema multiforme. Klin. M. f. Augenh., 1922, v. 68, pp. 216-220.
[38] Herbert, H. Preliminary note on the pathology and diagnosis of spring catarrh. Brit. Med. Jour., 1903, v. 2, p. 735. Clinical observations on spring catarrh. Brit. Med. Jour., 1907, v. 2, p. 1232.
[41] Lehrfeld, Louis. Allergic reactions in vernal conjunctivitis. Amer. Jour. Ophth., 1925, v. 8, pp. 368-373.
[42] ———. Vernal conjunctivitis; observations on 87 cases at the Wills Hospital, 1929-1931. Arch. of Ophth., 1932, v. 8, pp. 380-404.
[43] Zimmermann, E. L. The role of the arsphenamines in the production of ocular lesions. Arch. of Ophth., 57: 509-530, 1928, v. 50, pp. 509-530.
[44] Hegner, H. Severe necrosis of the cornea in salvarsan poisoning. Klin. M. f. Augenh., 1917, v. 59, pp. 624-636.
[45] Borel, G. A new palpebral syndrome. Bull. et mem. Soc. franc. d'Opht., 1933, v. 46, pp. 168-180.
[46] Morax, V. Conjunctival affections characterized by pseudomembranous exudates, corneal lesions and recidivating granulomas. Ann. d'Ocul., 1928, v. 165, pp. 401-421.
[47] Schuster, E. Membranous conjunctivitis of a month's duration. Ztschr. f. Augenh., 1924, v. 54, pp. 325-328.
[48] Castroviejo, R. Ligneous conjunctivitis; a new case. Arch. de oftal hispano-Am., 1935, v. 35, Dec., pp. 634-641.
[49] Uhthoff, W. A case of chronic pseudo-membranous conjunctivitis. Zehender M. f. Augenh., 1914, v. 18, pp. 228-229.
[50] Guibert. Chronic pseudo-membranous conjunctivitis; bacteriological examination. Arch. d'Ophth., 13: 627-630, 1893, v. 13, pp. 627-630.
[51] zur Nedden, M. Observations on 500 cases of epidermic keratoconjunctivitis. Klin. M. f. Augenh., 1940, v. 105, pp. 424-430.
[52] Bullowa, J. G. M., and Jacobi, M. Ulcerative laryngitis due to C. ulcerans. Amer. Jour. Dis. Child., Jan., 1931, v. 41, Jan., pp. 120-125.
[53] Ruediger, E. H. The occurrence of virulent pseudo-diphtheria bacilli in gangrenous tonsillitis and pharyngitis of scarlet fever. Trans. Chicago Path. Soc., 1903, v. 6, Nov. 9, pp. 45-49.
[54] Hamilton, Alice. The question of virulence among pseudodiphtheria bacilli. Jour. Inf. Dis., 1904, v. 1, pp. 690-713.
[55] Petrie, G. F., and McClean, D. The inter-relations of C. ovis, C. diphtheriae, and certain

diphtheroid strains derived from the human nasopharynx. Jour. Path. and Bact., 1934, v. 39, Nov., pp. 635-663.

[56] Gilbert, R., and Stewart, F. C. Corynebacterium ulcerans: A pathogenic microorganism resembling C. diphtheriae, Jour. Lab. and Clin. Med., 1927, v. 12, May, pp. 756-761.

[57] ———. Corynebacterium ulcerans: Its epidemiologic importance. Jour. Lab. and Clin. Med., 1929, v. 14, Aug., pp. 1032-1036.

[58] Dunphy, E. B. Membranous conjunctivitis. In Report of New England Ophthalmological Society. Amer. Jour. Ophth., 1934, v. 17, p. 850.

Discussion

Dr. F. H. Verhoeff (Boston, Massachusetts): I notice that every type of membrane that I have ever seen and some that I haven't are mentioned in the abstract, but a membrane that sometimes occurs in a condition we used to call scrofula doesn't seem to be included. One seldom hears that term used any more. We frequently used "scrofulous diathesis," in cases of children with enlarged glands. Probably tuberculous adenitis was always at the bottom of this condition. Some of those patients, instead of getting phlyctenular conjunctivitis, would have an inflammatory membrane on the palpebral conjunctiva. I wonder whether you are acquainted with such membranes?

It seems to me, several years ago, there was a paper given before this Society on a membranous conjunctivitis of infants. Did you see that?

Dr. M. J. Hogan (San Francisco): Yes, I did.

Dr. Verhoeff: Have you referred to that?

Dr. Hogan: Not in this paper.

Dr. Verhoeff: It was a very excellent paper. The conjunctivitis was of quite a severe type, as I recall it. It was often associated with the formation of a polypoid growth, wasn't it?

Dr. Hogan: Yes, sir.

Dr. Verhoeff: I noticed reference to experiments on the inoculation of pseudodiphtheritic membranes in the conjunctiva of animals. If you made such experiments with diphtheria bacilli, I am glad I wasn't around when you did so.

Dr. Hogan: We used diphtheria toxin only.

Dr. Verhoeff: You don't mention it here.

Dr. Hogan: I mentioned it in this abstract.

Dr. Verhoeff: I see. I couldn't hear you well enough to know whether you mentioned it.

Dr. Hogan: Morax, Elmassian, and Sourdille were able to produce membranous conjunctivitis with diphtheria toxin alone or by inoculation of the cultures of diphtheria organisms.

Dr. Verhoeff: I should not have feared being around when you used the toxin, but wasn't it a rather dangerous procedure in the laboratory to have diphtheria bacilli in the conjunctiva?

Dr. Hogan: We did not use the bacilli.

Dr. Verhoeff: I see. Well, perhaps you're lucky.

Dr. Hogan: I did not mention tuberculous membranes of the conjunctiva here, but it is discussed in the paper.

Dr. Verhoeff: And you didn't mention that type of membrane I was speaking about, did you?

Dr. Hogan: No, I eleminated the term scrofulous because I think probably some of those cases would be placed in other groups, either streptococcic or some other form of bacterial or toxic membranous conjunctivitis.

Dr. Verhoeff: I imagine you could put it under those, but we used to call it scrofulous.

Dr. Parker Heath (Boston, Massachusetts): You mentioned the word "trau-

matic," and I wish you would elaborate on trauma, with or without hemoglobin, forming a membrane.

DR. HOGAN: Most of the cases of membranous conjunctivitis which follow trauma are those in which a child or adult receives a laceration of the conjunctiva, with or without bleeding, in which the membrane forms. A localized membrane may form in the area of the laceration, which, as a transient membrane, of course, is dependent on the healing of the wound. Usually the wounds are clean, and the formation of a membrane depends on the formation of a fibrin clot within the wound itself.

DR. HEATH: There is a membrane, if I may speak once more, associated with hemoglobin which forms a second membrane, a real membrane, on top, which persists. It is not transient. Have you noted that?

DR. HOGAN (closing): No, I have not noticed that.

STUDIES ON THE PHYSIOLOGY OF THE EYE USING TRACER SUBSTANCES*

I. THE STEADY-STATE RATIO OF SODIUM BETWEEN THE PLASMA AND AQUEOUS HUMOR IN THE GUINEA PIG

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These studies were undertaken as part of a plan to investigate the permeability of mammalian membranes. The eye is a specially suitable organ for such studies because its fluids can be tapped without appreciably disturbing its normal state. As has been pointed out frequently[1, 2] the use of radioactive isotopes offers a unique method for permeability studies. In this first report we shall discuss the steady-state ratio of sodium between the plasma and aqueous humor and in the second report[3] we shall discuss the turnover rate of sodium between these two fluids and the methods of analyzing such data.

The steady-state ratio between the plasma and aqueous humor of sodium has been studied by classical chemical methods in several species but not in the guinea pig (table 1), and it is noted that there is little agreement concerning the ratio even in the same species. It is important that the ratio of sodium between the plasma and aqueous humor be accurately determined in order to understand the mechanism of formation of the aqueous humor. If there is an excess of sodium in the aqueous humor, this may be

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explained either by a secretory mechanism or by the loss of water from the aqueous through the cornea. In measurements in guinea pigs of the steady-state ratio using radioactive sodium (Na^{24}) as a convenient ultramicro method, we found the concentration ratio of plasma sodium to aqueous sodium to be lower than that reported for other species.

Methods

Radioactive sodium (Na^{24}) was prepared in the 60-inch cyclotron of the Department of Terrestrial Magnetism, Carnegie Institution of Washington. Metallic sodium, after deuteron bombardment, was dissolved as sodium alcoholate in 95-percent ethyl alcohol. Sodium chloride was precipitated by addition of concentrated hydrochloric acid. The precipitated sodium chloride was dissolved in water, filtered, dried on a hot plate to remove excess HCl, and the NaCl finally dissolved in a volume of water suitable for injection.

TABLE 1

DISTRIBUTION OF SODIUM BETWEEN THE PLASMA AND AQUEOUS HUMOR AS REPORTED IN THE LITERATURE

Author	Species	Plasma	Aqueous Humor Na. mgm. per 100 cc.	PL/AQ
Lebermann[4] 1925	Rabbit	470	320	1.47
Gaedertz and Wittgenstein[5] 1927	Dog	328	314	1.04
Tron[6] 1927	Ox	331	339	.98
Duke-Elder[7] 1927	Horse	145	121	1.20
Baurmann[8] 1929	Cow	326	337	.97
	Rabbit	303	317	.96
Stary and Winternitz[9] 1932	Horse	333	362	.92
Davson[10] 1939	Cat	162	156	1.03
Duke-Elder[11] 1936	Cat	160	150	1.07

Adult guinea pigs of mixed breeds, weighing between 500 and 1,000 gm., were used. The animals were fed rabbit pellets and fresh greens. Friedenwald and his co-workers have shown[12] that vitamin-C deficient guinea pigs have a lowered rate of formation of intraocular fluid. As a precaution against vitamin-C deficiency in our guinea pigs, each animal received 50 mg. of ascorbic acid 24 hours prior to the introduction of the tracer substance.

Three tenths of a cubic centimeter of an NaCl solution, containing about 1.336 mM/cc. was injected into the peritoneal cavity. After 24 hours, the aqueous was removed with a glass capillary pipette. Immediately thereafter a sample of blood was taken by cardiac puncture. Only brief ether anesthesia was necessary to carry out these procedures.

TABLE 2

EQUILIBRIUM RATIO PLASMA/AQUEOUS

No.	Pe* mM/kg·H_2O	Ae† mM/kg·H_2O	Pe/Ae
11	7.680	7.975	0.963
12	.82	.84	0.978
14	1.101	1.137	0.970
15	1.249	1.329	0.937
17	1.069	1.132	0.943
18	.888	1.011	0.878
21 A	1.253	1.365	0.917
27	7.32	7.76	0.943
28	6.45	7.46	0.865
C	5.62	6.14	0.914
K	.717	.755	0.953
	.717	.834	0.862
L	.714	.836	0.854
	.714	.784	0.912
			X=0.920 ±0.033

* Pe = equilibrium plasma.
† Ae = equilibrium aqueous.

The weight and radioactivity determination of plasma and aqueous were made in shallow weighing bottles of uniform dimensions. The aqueous was delivered from the pipette to a weighing bottle which was immediately covered. The blood was oxalated and centrifuged

and then 0.1 cc. of plasma was delivered to a weighing bottle. After determination of the wet weight of the aqueous and plasma samples, they were spread uniformly over the bottom of the weighing bottles by the addition of a measured amount of water. The samples were then dried and the dry weight determined.

Measurements of the radioactivity of the samples were made with a pressure ionization chamber connected to a string electrometer.[13]

Results

The beta particles per second per gram of aqueous water or plasma water were calculated and the concentration of tagged sodium was expressed in millimoles of sodium per kilogram of water. The average equilibrium ratio of plasma to aqueous was found to be $0.920 \pm \sigma = 0.03$ (table 1).

Discussion

The Donnan ratio of plasma to body fluid for sodium has been reported to have a theoretical value of 1.04 in dogs (Van Slyke) when all of the sodium in the plasma is ionized. Green and Powers[14] and Ingraham, Lombard, and Visscher[15] have shown by *in vivo* dialysis and by *in vitro* ultrafiltrates of dogs' plasma that proteins depress the activity of sodium in the plasma by binding it in a nondiffusible form. This removes approximately 8 to 11 percent of the sodium from consideration in the Donnan equilibrium and raises the theoretical value to around 1.12.

If we may transfer these values from the dog to the guinea pig, a considerable difference is evident between the theoretical and experimental ratio. The difference between the theoretical ratio of 1.12 in dogs and our reported ratio of 0.920 in guinea pigs may be due to several factors: (1) A species difference, (2) the passage of water from the aqueous through the cornea to the tears and the subsequent concentration of sodium in the aqueous, and (3) the secretion of sodium into the aqueous by the ciliary body or iris.

Summary

1. Radioactive sodium was used as a tracer to study the distribution of sodium between the plasma and aqueous and between aqueous and lens in the guinea pig.

2. The steady-state ratio; sodium plasma/sodium aqueous was found to be 0.920.

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References

[1] Hahn, L., and Hevesy, G. Acta Physiol. Scand., 1941, v. 1, fasc. 4, p. 347.
[2] Krough, August. Proc. Royal Soc. Biol., 1946, v. 133, pp. 140-200.
[3] Wilde, W. S., Scholz, R. O., and Cowie, D. B. Amer. Jour. Ophth., 1947, v. 30, Dec., pp. 1516-1526.
[4] Lebermann, F. Arch. f. Augenh., 1925, v. 96, pp. 355-384.
[5] Gaedertz, A., and Wittgenstein, A. Arch. f. Ophth., 1927, v. 118, pp. 738-744.
[6] Tron, E. Arch. f. Ophth., 1926, v. 117, pp. 677-692.
[7] Duke-Elder, W. S. The Nature of Intraocular Fluid. London, 1927.
[8] Baurmann, M. Ber. d. deutsch. ophth. Ges. 1928. Heidelberg, 1929, v. 47, pp. 156-169.
[9] Stary, Z., and Winternitz, R. Ztschr. f. physiol. Chem., 1932, v. 212, pp. 215-233.
[10] Davson, Hugh. Jour. Physiol., 1939, v. 96, pp. 192-201.
[11] Duke-Elder, Benham, and Davson. Jour. Physiol., 1937, v. 89, p. 61.
[12] Friedenwald, J., Buschke, W., and Michel, H. O. Trans. Amer. Ophth. Soc., 1939.
[13] Flexner, L. B., and Pohl, H. L. Amer. Jour. Physiol., 1941, v. 132, p. 594.
[14] Green, C. H., and Powers, M. H. Jour. Biol. Chem., 1931, v. 91, p. 183.
[15] Ingraham, R. C., Lombard, C., and Visscher, M. B. Jour. Gen. Physiol., 1933, v. 16, p. 637.

STUDIES ON THE PHYSIOLOGY OF THE EYE USING TRACER SUBSTANCES*

II. The turnover rate of sodium in the aqueous humor of the guinea pig: Methods of analysis

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One method of characterizing a membrane is to inquire whether the steady-state concentration gradient maintained across it is of such magnitude as would require the expenditure of energy locally in the membrane itself. This is essentially the method of our first paper in this series[7] in which we measured the steady-state ratio of sodium tagged with radiosodium (Na^{24}) between the plasma and aqueous humor of the eye of the guinea pig and inferred from this ratio that a considerable excess of free sodium is present in the aqueous humor of guinea pigs such that its maintenance might indeed require an expenditure of energy locally at the blood-aqueous barrier.

Another method is to measure the rate at which different solutes cross the membrane. One can then describe the permeability of the membrane with respect to the physicochemical properties of various ionic and molecular species. On may also study the effect upon the transfer rate of applying a number of different experimental conditions or chemical agents. For these, it is best to study the transfer of a naturally occurring constituent that is intrinsic to the medium bathing the membrane. The tracer technique is ideally suited to this in that one may work with a mere trace of material which does not upset normal ionic or molecular ratios.

We have attempted in the experiments to be reported here to gain a measure of the permeability of the plasma-aqueous barrier to sodium by determining the rate of transfer of sodium into the aqueous humor of the guinea pig using radiosodium (Na^{24}). Particular effort has been made in this initial work to analyze the difficulties involved in calculating rates from tracer data. The analysis is developed by describing two current approaches to the problem, the direct or linear,[2, 8] and the indirect or exponential methods.[5, 9]

The indirect method was used by Kinsey, Grant, Cogan, Livingood, and Curtis[3, 4] for data taken from the rabbit. Our treatment differs from theirs mainly in the more formal manner in which the exponential factors or constants are derived and interpreted. We are indebted to the paper of Merrell, Gellhorn, and Flexner[5]

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and to that of Silversmit, Entenman, and Fishler[9] for this approach.

Our result for the guinea pig is of the same order of magnitude as that of Kinsey and colleagues for the rabbit in that we estimate that the intrinsic sodium of the aqueous is renewed at the rate of one turnover every hour.

Experimental procedure

The methods of preparing a neutral solution of NaCl labeled with radiosodium (Na^{24}) and of sampling the aqueous and plasma are given in the preceding paper.[7] Less than 1 cc. of labeled solution was injected into a foreleg vein of the guinea pig under brief ether anesthesia. The animal was allowed to recover and brief anesthesia was again applied when the aqueous was collected. Blood was taken from the left heart by chest puncture. The blood was always sampled later than eight minutes after the intravenous injection of tracer sodium, at which time the labeled substance had reached a steady value in the circulating plasma (See Figure 2 taken from Merrell, Gellhorn, and Flexner[5]).

Data

The original data from which calculations or interpretations are to be made are shown in the first five columns of Table 1. The data from the aqueous are also plotted in Figure 1. On the ordinate, instead of plotting absolute concentrations of tracer, we place the proportion of its

TABLE 1

THE CONCENTRATION OF TRACER SODIUM IN AQUEOUS HUMOR AT STATED TIMES WHICH BEGAN WITH INTRAVENOUS INJECTION OF THE SODIUM LABELED WITH RADIOACTIVE Na^{24}

Animal No.	Time (Min.)	$A^*=n^*$ (mM/kg.)	$P^*_{eq.}$ (mM/kg.H_2O)	$A^*/A^*_{eq.}$	$\bar{P}^*$ (mM/kg.H_2O)	$fn^*/\bar{P}^*$	k
1	3.8	.515	3.16	0.152	8.33	.0575	.0151
	8.0	.886		0.255	5.68	.145	.0181
2	5.5	.372	2.76	0.126	5.70	.061	.0111
3	5.1	.450	5.47	0.076	11.82	.035	
	7.0	.843		0.143	10.25	.076	.0109
4	8.1	.682	2.60	0.243	4.58	.138	.0171
	15.1	.810		0.289	3.68	.205	
5	10.5	.790	2.36	0.312	3.74	.197	
6	20.5	.386	1.08	0.330	1.41	.254	
8	6.5	1.640	8.70	0.174	16.87	.090	.0139
9	210.0	1.483	1.59	0.868			
10	25.0	1.297	3.01	0.401	3.75	.321	
	46.0	2.080		0.643	3.41	.567	
I	33.5	4.630	9.100	0.473			
E	64.0	1.076	1.383	0.723			
26	76.0	0.712	0.907	0.730			
	91.0	0.733		0.751			
27	45.0	0.900	1.262	0.663			
	60.0	0.979		0.722			
28	12.5	1.840	7.425	0.234			
	39.1	3.600		0.452			
29	66.0	4.120	5.360	0.715			
	91.0	4.580		0.795			

Tracer sodium is expressed in millimoles per kilo aqueous ($A^*=n^*$) or per kilo of plasma water ($P^*_{eq.}$), in which the subscript "eq." refers to the steady-state value of tracer. To calculate $A^*/A^*_{eq.}$ the proportion of its equilibrium value attained by the tracer in the aqueous at the given time, it was noted that

$$\frac{A^*}{A^*_{eq.}}=\frac{A^*}{P^*_{eq.}}\left(\frac{P^*_{eq.}}{A^*_{eq.}}\right)=\frac{A^*}{P^*_{eq.}}\,f$$

in which $f=0.93$ was averaged from several guinea pigs used in our previous work.[7]

equilibrium value attained by the tracer in the aqueous at the time of sampling.

It is not at once apparent how one may calculate the rate of entry of intrinsic sodium from the rate of accumulation of tracer in the aqueous. Several basic difficulties present themselves. For instance, the measured accumulation of tracer is not a true picture of one-way inflow since some of the tracer which has entered during a finite time will have left the aqueous by outflow. Thus curves for the accumulation of tracer tend to bend toward the horizontal as time elapses and to approach an asymptotic value (fig. 1).

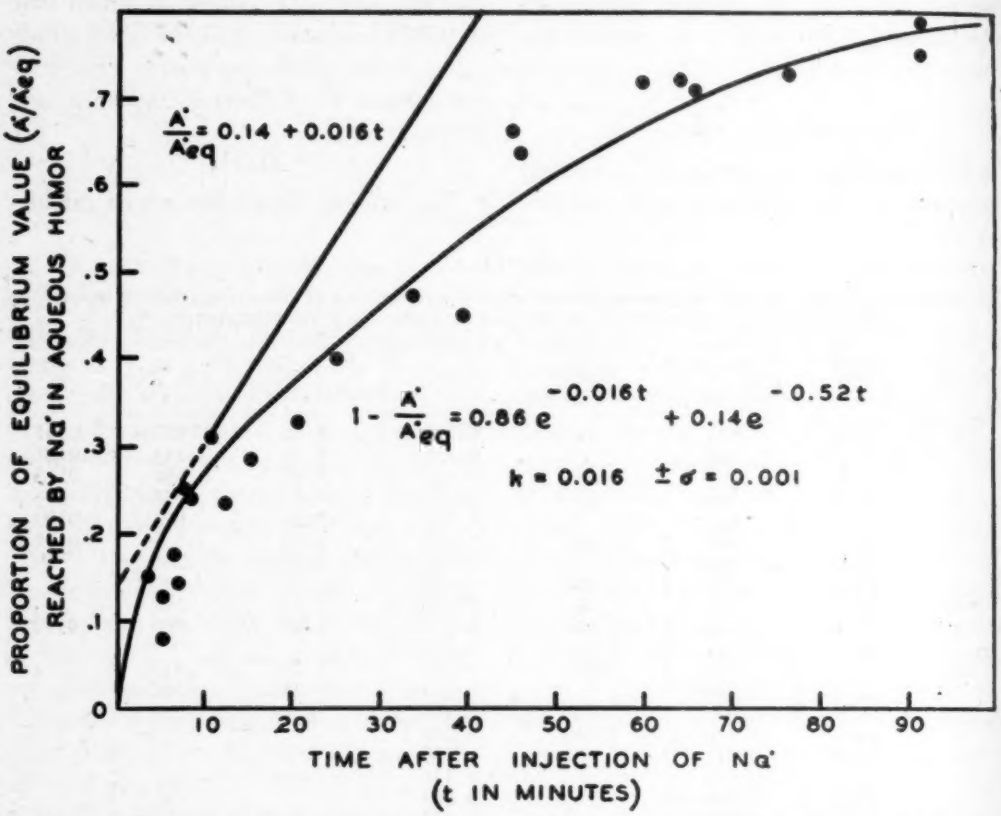

Fig. 1 (Wilde, Scholz, and Cowie). The dots represent the accumulated tracer sodium in the aqueous humor at given time after the intravenous injection of labeled sodium. The upper straight line represents prediction of labeled sodium by the direct method; the lower curve prediction by the indirect (exponential) method.

Under *Theory* we will discuss two fundamental methods of studying these difficulties.

Theory

In the first, the *direct method*, the amount of tracer accumulated in the aqueous is measured only early after its intravenous injection during which time very little of the tracer which has entered the aqueous has been lost again by outflow. In the second, the *indirect method*, the secondary outflow of tracer is accounted for in the mathematical treatment itself.

The direct method

In using a tracer substance to measure

transfer rate across a membrane, such as the plasma-aqueous barrier, it is assumed that tracer and intrinsic body substance are transferred across the barrier in quantities proportionate to their concentrations in the plasma bathing the barrier; that is:

$$\frac{P^*}{P} = \frac{\Delta n^*}{\Delta n}, \qquad (1)$$

in which P^* and P are the molar concentrations of tracer and intrinsic substance in the plasma at a given instant and Δn^* and Δn are the number of moles of the corresponding substances which during this same instant pass across the membrane from the plasma into the aqueous humor.

This theory holds only for the instantaneous passage of an infinitesimal quantity of tracer Δn^*. Only on two conditions can it be extended to measurements of finite amounts of accumulated tracer n^* in the aqueous. First, over long enough periods of accumulation some tracer can be expected to leave the aqueous by normal channels of outflow. Error in n^* due to this is minimized by collecting aqueous as soon as practicable after the intravenous injection of tracer. Second, once the tracer has been injected, its concentration in plasma P^* is, until equilibrium is reached, continually declining. We must substitute an average value $\overline{P}^*$ estimated from the area under a plasma time-concentration curve. Equation 1 with rearrangement then becomes:

$$\frac{n}{P} = \frac{n^*}{\overline{P}^*} \qquad (2)$$

in which n^* is the number of moles of tracer accumulated in a gram of aqueous during the period of observation and n is the number of moles of intrinsic substance which have passed into and out of this amount of aqueous in the same time. It is customary to express this as a fraction of the total substance A, the concentration, in a gram of aqueous. Thus, the fraction exchanged is n/A.

A number of substances reach a steady state or equilibrium ratio between plasma and aqueous. This can be symbolized as:

$$\frac{P}{A} = f \qquad (3)$$

If Equation 2 be multiplied by Equation 3, the value P in the left terms divides out, leaving the useful relation:

$$\frac{n}{A} = \frac{fn^*}{\overline{P}^*} \qquad (4)$$

Division by time t during which tracer is allowed to accumulate gives the exchange or turnover rate:

$$k = \frac{n}{At} = \frac{f\,n^*}{\overline{P}^* t} \qquad (5)$$

THE INDIRECT METHOD

The turnover rate k of a given intrinsic substance in the aqueous humor of the eye is defined as $k = r/A$, in which r is the number of moles of the substance which move by exchange into or out of a gram of aqueous per unit time (note that $r = n/t$ in the notation for the direct method) and in which A is the concentration in moles of the substance in a gram of aqueous. Since A is a constant, it follows that the rate r of movement of substance into the aqueous is equal to the rate r of movement of substance out of a gram of aqueous.

Hence, at any instant beginning from the time of the intravenous injection, the rate of one-way entry of tracer into a gram of aqueous is equal (1) to r, the number of moles of substance entering the aqueous per unit of time multiplied by (2) the proportion of this which is tracer, P^*/P. Meanwhile, the rate at which tracer is leaving the gram of aqueous is equal (1) to r, the number of moles of substance leaving the gram of aqueous per unit time, multiplied by (2) the pro-

portion of this which is tracer, A*/A.

Thus the net rate of accumulation of tracer is:

$$\frac{dA^*}{dt} = r\frac{P^*}{P} - r\frac{A^*}{A} \qquad (6)$$

in which P and P* are the moles of substance and tracer in a gram of water of the fluid bathing the plasma-aqueous barrier and A and A* are the respective values for a gram of aqueous humor.

This equation is simplified by noting at once that r/A is the turnover rate k and that r/P can be expressed in terms of k. For most substances, A/P = f′ is a constant, an equilibrium ratio across the aqueous barrier. Thus r/P may be set equal to r/A × A/P = kf′.

With these substitutions and rearrangements Equation 6 becomes:

$$\frac{dA^*}{dt} + kA^* = f'k\,P^* \qquad (7)$$

During the first few minutes after intravenous injection of tracer, it remains unknown whether the concentration P* of tracer presented to the aqueous barrier is (a) identical to that in the plasma or (b) whether P* is some lower value due to dilution of tracer in a pool of interstitial fluid interposed between the plasma-bearing capillaries and the aqueous barrier itself.

The remainder of the discussion will be limited to a study of the data obtained by using radiosodium (Na^{24}) in the guinea pig.

In case (a) in which P* is represented by plasma values of tracer sodium, an integral for P* may be substituted into Equation 7 in a form taken directly from Merrell, Gellhorn, and Flexner.[5] This is represented in the upper curve of Figure 2 for which $P^* = a\,e^{-b\,t} + P^*_{eq.}$ (see notation in legend of figure 2).

With this substitution, Equation 7 is a linear differential equation of the first order (ref. 1, p. 19). Integrating, solving for the constant of integration, and rearranging after substitution of $A^*_{eq} = f'P^*_{eq.}$, where $A^*_{eq.}$ and $P^*_{eq.}$ are equilibrium values for tracer sodium per gram of aqueous and per gram of plasma water respectively, gives:

$$1 - A^*/A^*_{eq.} = (1 + L)\,e^{-kt} - L\,e^{-bt} \qquad (8)$$

in which L = k/ (k-b) times $a/P^*_{eq.}$ is a constant.

For case (b), it is desired that the integral substituted for P* represents the concentration of tracer sodium actually present in the interstitial fluid bathing the aqueous barrier. During the first eight minutes, after the intravenous injection, while tracer sodium is rapidly entering the interstitial fluid from the plasma, the concentration in the interstitial fluid may first rise abruptly and then decline to equilibrium $P^*_{eq.}$. Such a situation would be complex to describe mathematically. We will consider the simplified case in which during the early eight minutes leading to equilibrium in the plasma the tracer which has left the circulating plasma up to any given instant is uniformly mixed in the total volume of interstitial fluid in the guinea pig. The equation for P* in this situation can be derived either by simple visual inspection of the lower curve of Figure 2 or by a more formal treatment analogous to that used by Merrell, Gellhorn, and Flexner for the plasma curve.

If now this substitution, $P^* = P^*_{eq.} - P^*_{eq.}\,e^{-bt}$, is made into Equation 7, an integration procedure analogous to that used for Equation 8 yields the equation:

$$1 - A^*/A^*_{eq.} = (1 - M)\,e^{-kt} + M\,e^{-bt}, \qquad (9)$$

where M = k/k-b is a constant. (In this derivation, we neglect a Donnan ratio across capillary membranes and assume that the concentration of sodium in plasma water is equal to that in interstitial fluid water.)

Results

The direct method

The quantity of intrinsic sodium exchanged in the aqueous during an experiment (equation 4) is $n/A = f\ n^*/\bar{P}^*$. The ratio $f = P/A = P^*_{eq.}/A^*_{eq.}$ was measured in a separate experiment as an average from several animals in which tracer sodium was allowed 24 hours after intraperitoneal injection to reach equilibrium between the plasma and aqueous.[7] In the rate experiment itself the value n^* is measured directly from the given sample of aqueous. $\bar{P}^*$ is estimated as follows: The decline in plasma concentration of tracer sodium P^* from the time of intravenous injection until the equilibrium point, beginning in the plasma about eight minutes after injection, is shown in the upper curve of Figure 2. This curve from Merrell, Gellhorn, and Flexner will be called a "standard curve" and was fitted to points from a number of animals, each point being adjusted to an assumed or arbitrary standard dose of tracer sodium.

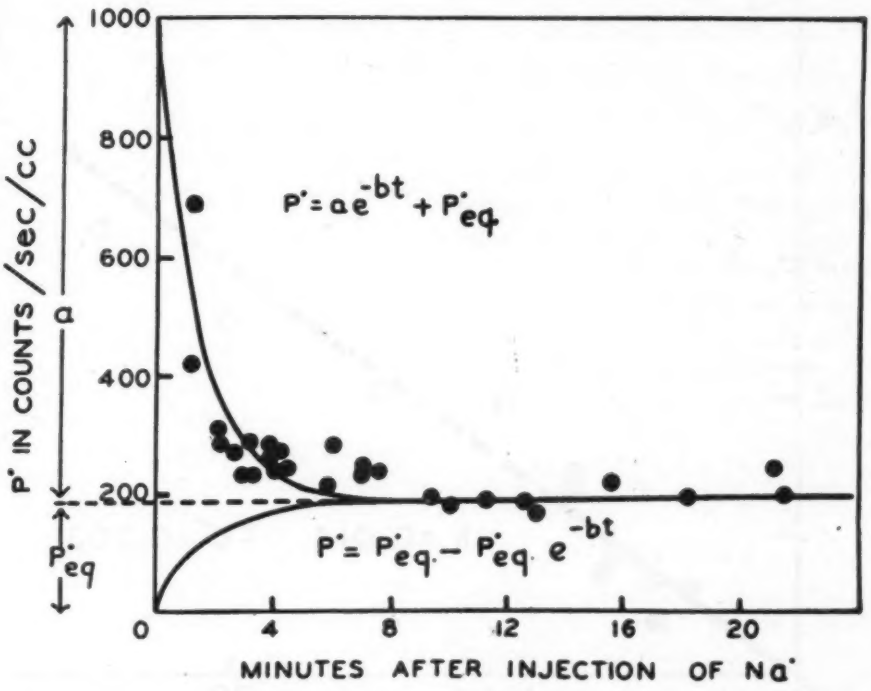

Fig. 2 (Wilde, Scholz, and Cowie). The concentration of tagged sodium (P^* in counts per sec. per cc.) in plasma plotted against time after injection of Na* into a foreleg vein of guinea pigs. The plotted data, the upper equation, and fitted curve are from Merrell, Gellhorn, and Flexner.[5] The lower equation and curve represent concomitant "average" concentrations in interstitial fluid (see explanation in text). The transformation from our notation to that of Merrell *et al.* is as follows: $P^* = c_t$, the concentration of labeled sodium in the plasma. $a = c_o - c_{eq.}$, in which c represents concentration of labeled sodium in plasma: c_o, at zero time and $c_{eq.}$ at equilibrium in the plasma. As shown by the arrow at the left, a is the concentration of tracer in the plasma at zero time as an "excess" over the equilibrium value in plasma. b is the rate of loss in concentration of plasma tracer substance per minute relative to excess concentration. $P^*_{eq.} = c_{eq.}$. In the symbols on the chart dots are used as superscripts in place of asterisks to identify tracer (for instance $P^{\cdot} = P^*$).

$\bar{P}^*$ is the average concentration of

plasma tracer presented to the aqueous barrier during the period t allowed for accumulation of n* amount of tracer. For the standard animal it would be the area under the curve divided by time t. This standard $\overline{P}^*$ and the $\overline{P}^*$ for an animal given a particular dose would be related

f $n^*/\overline{P}^*$ increases linearly with time the secondary loss of tracer from the fetus by outflow back to the mother is negligible. This early linearity for the aqueous is illustrated in Figure 3. It is not clear just where on the plot the linear period ends. Thus for reasons to be discussed later we

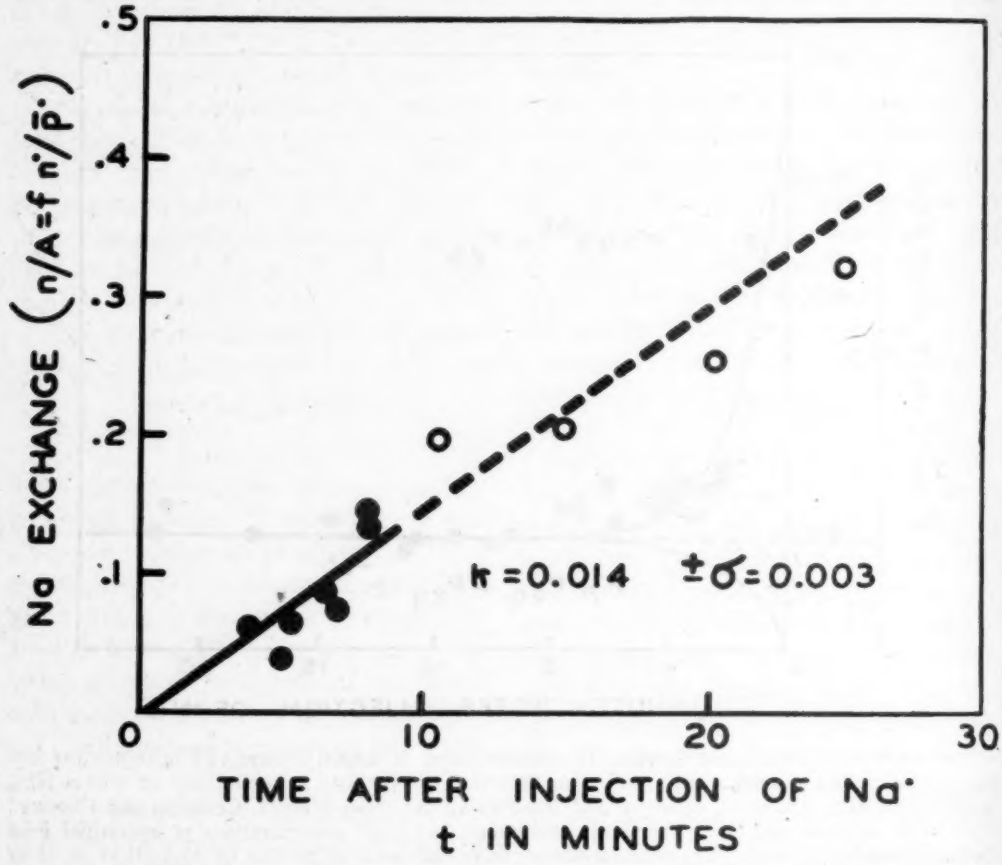

Fig. 3 (Wilde, Scholz, and Cowie). The direct or linear method. The apparent amount n/A of intrinsic aqueous sodium which had exchanged beginning from the intravenous injection of Na* until the stated time. Both circles and dots are experimental points but only the dots were used to calculate turnover rate, $k = fn^*/\overline{P}^*t$, as in Table 1. The average k value from these gives the slope of the continuous line drawn arbitrarily through the origin. This line is extended (broken) to show the divergence of later points (circles) because of outflow of tracer from the aqueous.

to each other as are the equilibrium concentrations $P^*_{eq.}$ of each.

Values of $n/A = f\, n^*/\overline{P}^*$ as calculated from Table 1 are plotted in Figure 3.

We have assumed in the studies of placental transfer rate done in this laboratory[2, 8] that as long as the value of

have arbitrarily chosen only points measured earlier than eight minutes after injection to calculate k from Equation 5 in which $k = f\, n^*/\overline{P}^*\, t$. The average k for the six animals chosen from Table 1 is 0.014 with a standard deviation of 0.003. This $k = n/At$, which is the turnover

rate, has been used as a slope to draw a line arbitrarily through the origin of Figure 3.

The turnover time corresponding to this k or slope would be 1/0.014 = 71 minutes for a complete turnover of intrinsic aqueous sodium.

The indirect method

Equation 8 predicts the value of $A^*/A^*_{eq.}$, the concentration of tracer in the aqueous at a given time as a proportion of the concentration in the aqueous at equilibrium. Values of $A^*/A^*_{eq.}$ estimated from the data of Table 1 are plotted in Figure 1. To fit the theoretical curve to these points the usual device a plot of ln $(1-A^*/A^*_{eq.})$ against time is considered. While this at first sight seems complicated by the presence of two exponentials, further examination reveals that one of these, that containing e^{-bt}, approaches zero at eight minutes, the time at which the plasma tracer approaches a steady value. Thus after eight minutes this term drops out and the log of the remaining part yields the linear relation.

$$\ln (I-A^*/A^*_{eq.}) = \ln (1 + L) - kt \qquad (10)$$

A plot of actual ln $(1-A^* /A^*_{eq.})$ values indeed demonstrates that the data fit such a linear relation for times later than eight minutes. A line fitted to these later points by least squares has the slope −0.016 which is the value of k or the turnover rate per minute. The standard error of estimate (ref. 6, p. 456) of this slope or rate is 0.001. The turnover "time" is thus 1/0.016 or 62.5 minutes.

If the straight line portion of this log curve is projected leftwards to the y axis it has the intercept value ln (1 + L) as indicated in Equation 10. Thus (1 + L) has the numerical value 0.86, which is the value of the coefficient of e^{-kt} in Equation 8. With 1 + L = 0.86, L = 0.14, the coefficient for e^{-bt}.

There remains the calculation of the value of b. Since L = k/ (k-b) times $a/P^*_{eq.}$, in which k = 0.016 and $a/P^*_{eq.}$ = 4.525, the latter being supplied by the paper of Merrell, Gellhorn, and Flexner,[5] b is calculated to be 0.52.

After substituting into Equation 8 the various values for the constants which have been enumerated above we have,

$$1-A^*/A^*_{eq.} = 0.86\, e^{-0.016\, t} + 0.14\, e^{-0.52\, t}$$

This equation was used to calculate points through which the lower curve of Figure 1 is drawn.

Equation 9 can be fitted by a device analogous to that used for Equation 8. When this is attempted, however, the fitted curve falls far below the experimental points. This implies that the early concentrations P* of tracer at the functional aqueous barrier are nearer those of the simultaneous declining values in the circulating plasma itself than they are to the ascending values averaged for interstitial fluid as a whole.

Discussion

Error in the direct method caused by tracer outflow. We have mentioned the effect upon the direct method of the outflow of tracer from the aqueous humor. We now show graphically how this error increases with time following the injection of tracer. The lower curve in Figure 1 shows the actual amount, as a fraction of equilibrium, $A^*/A^*_{eq.}$, of tracer in the aqueous at given times. This, as stated, was plotted from Equation 8 which accounts for outflow. The upper line, on the other hand, predicts the amount of tracer, expressed as $A^*/A^*_{eq.}$, which has entered the aqueous one-way, no account having been made for loss by outflow.

The distance between the curves in Figure 1 represents the error of the direct method due to outflow of tracer. At about eight minutes, when $A^*/A^*_{eq.}$ = 0.25, when tracer in the aqueous has attained

one fourth of its equilibrium value, the aqueous will have lost by outflow an amount of tracer equal to 11 percent of the tracer in it at that time; when $A^*/A^*_{eq.} = 0.4$, the discrepancy is 24 percent.

In calculating k by the direct method we have thus arbitrarily chosen only points sampled before eight minutes so that the error of outflow would be kept below 10 percent. The direct method gave a k value of 0.014 compared to 0.016 by the exponential method.

The simplicity of fitting the exponential. As one or another experimental condition or agent is tested for its effect upon the turnover rate, it is possible that the agent will be found to change the shape of the plasma curve. To apply the direct method might thus involve the detailed construction of the plasma curve for each agent. To avoid this, as is possible in the exponential method, is a distinct advantage. In the latter method one merely determines approximately how early a steady value is reached by tracer in the plasma. Aqueous values determined later in time may then be plotted as ln $(1-A^*/A^*_{eq.})$ to determine the slope $-k$, the turnover rate. If it is desired to draw the exponential curve, b can be calculated as previously indicated from the expression for L.

Aqueous values thus measured late in time are of greater magnitude and are more accurately measured than are the smaller early values required in the direct method.

However, warning must be given concerning the collection of data for calculating $A^*/A^*_{eq.}$ from A^*. We have shown in the legend of Table 1 that $A^*/A^*_{eq.} = A^*f/P^*_{eq.}$ Thus, the plotted value $A^*/A^*_{eq.}$ involves three errors: the error in A^* and that in $P^*_{eq.}$ for the particular animal and the deviation represented by the difference in f as averaged from a series of animals and the f ratio for the particular animal. The effect of this summated error becomes particularly significant if $(1 - A^*/A^*_{eq.})$ approaches zero, at time near equilibrium. Then its ln value experiences large deviation for small deviation in $A^*/A^*_{eq.}$. One should work with well-scattered points but along the middle range of the time course of the equilibration process for the aqueous.

The effect of early unknown time—P values on the direct method.* Precise application of the direct method requires accurate values at known times for the concentration of tracer sodium P^* in the interstitial fluid at the effective barrier to the anterior chamber. To avoid error from outflow of tracer, sampling of the aqueous humor must be done early after the intravenous injection of tracer. This is just the time, during the early decline of plasma tracer, when it is most difficult if not impossible to measure or calculate the value of tracer at the barrier. Furthermore, depending upon the particular channel postulated for the entry of sodium into the anterior chamber, there may be a considerable time lag between the passage of tracer across the barrier and its delivery into the anterior chamber where we sample and measure it. For instance, if sodium enters the aqueous by way of the ciliary body the time for travel from the ciliary body through the posterior chamber and pupil into the anterior chamber where sampled would constitute a considerable portion of the short period allowed for accumulation of tracer in the linear method. These constitute unavoidable errors in the direct method as applied to aqueous.

The indirect method, on the other hand, is deliberately applied late after the injection. At this time P^* is a steady value in the plasma and probably in the interstitial fluid and the posterior chamber, if this latter constitute a pathway of entry

of sodium into the anterior chamber. The slope of the ln plot of $(1—A^*/A^*_{eq.})$ constitutes a proven value for k the turnover rate as we have defined it. This k refers to the average rate of the continual passage of intrinsic sodium through a gram of aqueous in the anterior chamber irrespective of the number and nature of the various channels by which sodium may traverse that chamber. The rate is, of course, expressed as a fraction of the total amount of intrinsic sodium in the unit of aqueous.

In the exponential equation itself the effect of the early uncertain P* values upon the delivery of tracer to the anterior chamber is summarized complexly in the constant L and the exponential factor b.

Summary

The direct or linear is compared with the exponential method of calculating from tracer data the turnover rate of a constituent in the aqueous humor of the eye. In the former, outflow of tracer from the aqueous is ignored; it being minimized by measuring the tracer accumulated in the aqueous only early after its intravenous injection.

A double exponential equation is fitted which accounts for the outflow as well as for the changing inflow of tracer which attends the declining plasma concentration that follows early after intravenous injection of tagged substance.

Tracer sodium tagged by radioactive (Na^{24}) was injected into the foreleg vein of guinea pigs. In six aqueous samples treated by the linear method the turnover rate was 0.014 ± 0.003; in 21 samples calculated by the exponential the rate was 0.016 ± 0.001. The latter represents a turnover time of 62.5 minutes.

By comparison with the exponential it is shown that the error for the linear method due to outflow is 11 percent by the time the tracer has reached one fourth of its equilibrium value in the aqueous.

Other disadvantages of the linear method not encountered by the exponential as applied to aqueous include: uncertainty concerning the exact value of the early concentration of tracer at the functional aqueous barrier; the error of measuring *small* amounts of accumulated tracer early after the injection; the necessity of precise construction of plasma time-concentration curves for tracer.

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References

[1] Cohen, A. An Elementary Treatise on Differential Equations. New York, D. C. Heath and Co., 1906, p. 19.
[2] Flexner, L. B., and H. L. Pohl. Amer. Jour. Physiol., 1941, v. 132, p. 594.
[3] Kinsey, V. E., Grant, W. M., Cogan, D. G., Livingood, J. J., and Curtis, B. R. Arch. of Ophth., 1942, v. 27, p. 696
[4] Kinsey, V. E., and Grant, W. M. Jour. Gen. Physiol., 1942, v. 26, p. 131.
[5] Merrell, M., Gellhorn, A., Flexner, L. B. Jour. Biol. Chem. 1944, v. 153, p. 83.
[6] Pearl, R. Introduction to Medical Biometry and Statistics. Philadelphia, W. B. Saunders Co., 1940, p. 456.
[7] Scholz, R. O., Cowie, D. B., Wilde, W. S. Amer. Jour. Ophth., 1947, v. 30, pp. 1513-1515.
[8] Wilde, W. S., Cowie, D. B., and Flexner, L. B. Amer. Jour. Physiol., 1946, v. 147, p. 360.
[9] Silversmit, D. B., Entenman, C., and Fishler, M. C. Jour. Gen. Physiol., 1943, v. 26, p. 325.

Discussion

Dr. Vesey (New York): I would like to ask the speakers if they made any efforts to observe the route of the outflow of the aqueous tracer substances from the anterior chamber.

Many arguments could be brought up.

Dr. Troncoso has beautifully shown that the lower animals, on which the experiments are usually carried out, do not have a structure resembling the human ciliary body. He showed that carnivora and rodentia do not have a ciliary body similar to that of human beings. They have a spongy tissue in the ciliary body, and this is the organ that carries the outflow of the aqueous in these animals. In human beings, as I said, many arguments could be brought up against the idea of the ciliary body being the main organ of the outflow, and if any research workers make any efforts to show the route of the outflow, I think our knowledge of the physiology of this very important subject would be enhanced quite a bit. I would like to hear something about that.

DR. WILDE: Well, we have one provisional observation that bears on that question. We have observed, in studying the rate of sodium flow into the lens, that the lens appeared to pick up more sodium than it should had it been bathed in tracer as we measured it in the anterior chamber. In other words, the lens had early been exposed to a tracer concentration higher than that found in the anterior chamber.

This could mean that an early rich batch of tracer was being delivered to the posterior chamber of the eye, and that this rich material was bathing the lens. Of course, it is to be admitted that sodium may have been crossing from the vitreous behind—not saying how quickly it may enter the vitreous. Dr. Scholz may have other comments in this regard.

DR. SCHOLZ: The only other thing that I have to add is that the technique we were using was not directly adaptable to determining the route of outflow—there are other radioactive techniques that might be used but we have not as yet employed them.

DR. DUNNINGTON: Are there any other questions?

DR. WILDE: One other comment in regard to the possible path of flow of tracer into the anterior chamber is that we have entertained the possibility that if the tracer did come by way of the ciliary body, there would be a considerable lag in time as this material went from the ciliary body to the anterior chamber by this pathway.

If I may refer to Slide 6 again, you will see that there is a suggestion of a peculiar early delay. This is only a very provisional type of data, however, in an animal as small as the guinea pig, and when the samples are so small. There is an indication of some delay; perhaps, low values, too early in time, or a tendency to pile up here. Dr. Friedenwald lately has entertained another equation in which it is attempted to account for a stepwise flow of tracer from, say, ciliary body to posterior chamber, and from posterior chamber into anterior chamber, having three exponentials in attempting to explain a problem of that sort. We are greatly indebted to Dr. Louis Flexner and Dr. Jonas Friedenwald for their advice, encouragement, and assistance with this work.

THE SODIUM-VAPOR LAMP AND ITS USE FOR REFRACTION*

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The use of selected portions of the spectrum in ophthalmology is not new. It was early evident that the ill-defined appearance of the eyeground by "white" light was due, in large extent, to the chromatic aberration of the human eye. This led inevitably to elimination of more or less of the polychromatic character of the illumination to obtain an improved fundus picture for certain specific details.

As early as 1903, Mayou[1] employed the mercury-vapor lamp. Vogt[2] utilized the carbon arc, supplemented by elimination of the infrared end through use of a 30-percent copper-sulfate solution with an added 1 percent of erioviridin to remove the visible red and orange. Friedenwald[3] also advocated the use of the carbon-arc lamp and introduced a filter to eliminate all but the yellow and green. Cousin[4] and Bichelonne[5] further limited the spectral range through filtration of an incandescent tungsten filament to hold the light source at about 5,800 A. U. The first use of sodium light as a monochromatic source occurred with Kleefeld,[6] in 1935. In all of these various spectral range selections, the light may be considered as "red free," but this is obviously a term of great freedom.[7]

Mayou's mercury-vapor lamp is completely red free but quite rich in the short blue and violet. Under it the fundus appears bluish gray, and the retina, because part of the transmitted spectrum is absorbed and part reflected in a diffused manner, appears largely opaque. Deeper structures cannot be seen as distinctly as is possible with more nearly monochromatic illumination.

Vogt established the carbon arc together with filtration of the infrared, red, and orange regions, to demonstrate the presence of the yellow pigment of the macula lutea in the living eye, and not solely as a postmortem phenomenon. As late as 1924, his "red free" light was still being used almost exclusively as a selective source of illumination.

Friedenwald in that year believed that "the full value of the control of spectral range of the light used in ophthalmoscopy has not yet been realized." He decided on the use of yellow light because this light is most strongly reflected from the fundus.[8] For his purpose, it proved advantageous to include some of the yellow-green portion of the wave band to enhance the visibility of certain fundus structures. Friedenwald's filter was a solution of aniline green Naphthol B in glycerin, and with the resultant illumination, the eyeground appeared yellow green, the venous blood as black, and the arterial blood as dark gray. After adaptation, connective-tissue streaks, vessel walls, and exudates appeared in shades bordering on white.

Cousin, Monnier, and Mouton,[4] in 1933, attempted to prove that yellow headlights on automobiles were superior not only to penetrate fog, but for increased visibility in clear atmosphere. They demonstrated that a certain black object which could be recognized at 130 meters with ordinary headlights was visible at a distance of 160 meters with their selective light. Their bulb contained a tungsten filament at 2,800°C. The filter, consisting of cadmium-sulfate solution, transmitted nearly monochromatic (98 percent) light of 5,820 A. U.

* From the Department of Ophthalmology, Northwestern University Medical School. Aided by a grant from B. Spero for the Sanford R. Gifford Memorial Fund. Read at the meeting of the Chicago Ophthalmological Society, May 19, 1947.

These investigators also used their bulb as illumination for a test chart provided with Snellen letters and Landolt broken circles to ascertain if this light increased visual acuity as well as improving visibility. They reported a 10-percent increase in visual acuity but did not detail how they had arrived at this figure; they also were under the impression that the eye would not so easily become fatigued under yellow illumination, and that its use in factories where detail work had to be done would therefore be advantageous.

In conclusion, they stated that selective yellow light could serve a twofold purpose to the ophthalmologist. It would be superior as source of illumination for test charts, as well as an ophthalmoscopic lamp, since it was less annoying when used for focal illumination. Moreover, the pupil did not contract as much as with ordinary light, and, consequently, fundus details could be made out more easily when a mydriatic was not used. The same light also proved superior for fundus study in cases with cloudy media because of its greater penetrating power.

Bichelonne, Favory, and Bégué[5] repeated some of the investigations just discussed. Once more, they reported visual acuity increased one tenth, and, again, no specific data as to how they arrived at that figure. They believed the increased visual acuity to be explained by the fact that yellow light omitted the short end of the spectrum. André Broca[9] had previously demonstrated the increased retinal fatigue accompanying the shorter wave lengths; according to his work the optimum wave length for minimal fatigue would be 5,600 A. U.

With yellow light as source of illumination, fundus details appeared much more distinct; in particular, the retinal vessels stood out very clearly as did retinal and choroidal changes. These authors also believed that there should be gratifying results with vitreous opacities, but published their article before substantiating that belief clinically.

Although the filters in all these investigations provided fairly monochromatic yellow light, it is surprising that the sodium-vapor lamp had not been employed before as the one light source that filled, most ideally, this requirement. Certain forms of this type of lamp were available for more than a decade, the first attempts reaching back to 1919 when A. H. Compton of the Westinghouse Company applied for a patent.[10] Kleefeld[6] had been experimenting with infrared light and its application to fundus study. Technical reasons slowed up his progress and, in an endeavor to turn his research efforts into more promising fields, he was the first one to employ the sodium-vapor lamp in ophthalmology, investigating its possible advantages for focal illumination, retinoscopy, examination with the plane mirror, indirect and direct ophthalmoscopy, and photography of the anterior segment. So far as retinoscopy was concerned, the reflected light appeared grayish white. The reflex was very distinct and one was not forced to observe it in the area of the disc, as in retinoscopy with ordinary light. It was quite easy to perform retinoscopy in the foveal region (obviously, Kleefeld performed his retinoscopies without cycloplegic).

This author's statements are quite enthusiastic, listing numerous advantages, and possibly creating the impression that he would prefer to replace the ordinary polychromatic light with the sodium lamp.

Serr,[11] who repeated some of Kleefeld's studies, was much less enthusiastic in his conclusions. He found the direct method of ophthalmoscopy unsatisfactory (naturally he had to use a nonilluminating type of ophthalmoscope), and his findings are based on results obtained by indirect ophthalmoscopy.

Serr reported that where opacities of the refractive media existed, it was still possible to obtain a fairly distinct view of the fundus where polychromatic light allowed only a vague glimpse. This characteristic of sodium light was expected, since the refracting media become more transparent as the wave length increases.[12] Furthermore, sodium light was particularly suited to old people since the yellow-brown discoloration of the lens did not absorb this light to any extent. Of course, even sodium light did not permit visualization of the eyeground where the opacities exceeded a certain intensity.

Serr further reported that in instances of corneal scars, fresh infiltrates of the cornea, extensive deposits of keratic precipitates in uveitis, exudates, and fibrinous deposits on the anterior surface of the lens, as well as vitreous opacities and hemorrhages, surprisingly many fundus details could be seen with sodium light against only an indistinct outline of the optic disc with white light. Serr found that sodium light penetrated living tissue, like the pigment epithelium, making choroid vessels appear distinct. There was a wide zone missing in the yellow portion of the absorption spectra of hemoglobin and oxyhemoglobin. Since, ordinarily, their walls were transparent, the retinal veins and arteries appeared black or gray respectively. For this reason, irregularities in the caliber and formation of anastomoses were brought out very distinctly. Likewise, hemorrhages and pigment deposits stood out very clearly—although it was not possible to differentiate them by their color but only by their configuration. In retinal detachment, a tear, appearing gray, could readily be differentiated from the black of a hemorrhage. Unlike the red-free light of Vogt, sodium light did not allow observance of the yellow color of the macula lutea.

With this light the retina was completely transparent, there were no reflexes, and not even the nerve fibers could be traced. The choroid absorbed a large part of the light; whatever portion reached the sclera was reflected and underwent further absorption on its return passage giving the choroid a grayish appearance. Serr observed evidence of choroidal hemorrhages in almost every case of severe contusion of the globe which could not be visualized by other means—not even the "red-free" light of Vogt.

Ballantyne,[13] during a visit of the British Ophthalmological Society to the Research Laboratory of G. E. C. Wembley in 1936, became acquainted with the sodium-vapor lamp and its possible use for ophthalmoscopic work. His conclusions, drawn from investigations made simultaneously but without knowledge of that by Kleefeld, were most complete and illuminating. His report agreed with those of other authors already mentioned, except that, contrary to Serr's statement, Ballantyne was under the impression that the course of the nerve fibers radiating from the disc could usually be fairly clearly traced. He stressed very emphatically that color values could not be appreciated in sodium light. The pigmentary changes in myopia, for example, were transparent, and a melanoma of the choroid disappeared under sodium light.[14]

Glueck,[15] contrary to a majority of opinions, believed that corneal opacities, as a rule, would not become more transparent with sodium light. Those resulting from interstitial keratitis were the exception, and he considered this fact as of almost diagnostic significance. Glueck did not mention a universal increase in visual acuity, but noted that patients with opaque media could see better when test types were illuminated with sodium light. He usually succeeded in enabling the patient to gain "a degree" in reading the test types by use of sodium light. He further

stated quite emphatically that he could see no advantage of sodium light in skiascopy but neglected giving reasons for these conclusions which were exactly contrary to Kleefeld's experience.

From the discussions so far, it is quite evident that in none of the previous investigations was the primary object to study the possible implications of the use of sodium light as a source of illumination in retinoscopy. Illumination of the test objects was done only in a very cursory manner. There was only a certain curiosity to see "what would happen" if sodium light was used. It is surprising that sodium light has not been investigated more thoroughly in connection with retinoscopy since, for theoretical reasons that have not heretofore been stressed, it seems to be singularly suited for this.

The human eye is not an achromatic optical instrument, as was first noted by Wollaston, in 1801. The amount of chromatic aberration has been variously reported as 1.3D. by Young, 1.5 to 3.0D. by Fraunhofer, and 1.8D. by Helmholtz.[16] Under ordinary conditions, this aberration does not interfere with clear vision; in fact, it requires special arrangements to demonstrate this phenomenon.

In ordinary daylight, the human eye supposedly focuses for the yellow part of the spectrum.[17] Thus it is myopic for the shorter wave length of the spectrum and hyperopic toward the red end. The most widely accepted explanation for this is that the yellow part of the spectrum is appreciated subjectively as its brightest portion, and that, in decreased illumination, relative brightness shifts toward the yellow-green region. A number of subjective methods for refraction are based on the chromatic aberration; for instance, the cobalt-glass test and its various modifications, and Brown's duochrome test. The principle of these tests is to offer two fields, the one illuminated by shorter, the other by longer, wave lengths than the yellow. It is impossible to have both fields in focus simultaneously. However, when both of them appear equally distinct—more correctly, equally blurred—the yellow supposedly is in exact focus. These methods are widely used among refractionists, and have proved to be valuable assets. Yet it seems that it would be more logical and more practical to use light of the specific wave length in which we are interested than to obtain our result by "interpolation."

In retinoscopy, interpretation of the refractive state of the eye is based on that portion of the spectrum that is reflected from the fundus; that is, light above 5,760 A. U.[15] Still that leaves a large portion of the spectrum subject to a chromatic aberration of possibly one diopter. Furthermore, subjective vision should be more distinct with sodium light as the source of illumination, and it should be much easier for the patient to decide exactly what spherical correction gives the best visual acuity. If this holds true for distance vision, it should be even more decisive at close range. Whereas the patient has to accommodate for the exact distance at which the test chart is presented when only monochromatic light is available, it is possible that with polychromatic illumination little or no accommodation is called into action if the violet portion of the light reflected from the reading chart is utilized at reading distance.

In an emmetropic eye (or one that is made emmetropic by correcting lenses) the punctum remotum for the short end of the spectrum is approximately 23 inches, which means that only ¾ myodiopter of accommodative effort would enable an individual to read at 16 inches with complete comfort. For the same result 2½ myodiopters of accommodation are required for the sodium line of 5,900 A. U.

It is known that there is such a phenomenon as "paradoxical" accommodation. Patients with aphakic eyes surprisingly often are able to read quite well at close range with their distance correction. The interpretation for this phenomenon is that these eyes utilize the violet end of the spectrum.

The investigations about to be discussed were undertaken to determine whether or not elimination of chromatic aberration would bring about improvement in our present method of refraction.

Procedure of Investigation

Source of Light

The Gates sodium-vapor unit, manufactured by the George Gates Company in Long Island City, New York, was selected as the source of light. The model equipped with a reflector for illumination purposes was used and, when further provided with a metal screen with a small hole in the center, served as retinoscopy light for a nonluminous retinoscope as well (fig. 1).

Strictly speaking, this lamp is not monochromatic, but the maximum output is between 5,889 and 5,895 A. U. Some of the other wave lengths emitted fall outside the visible spectrum, and need not be considered here. The remaining 2 percent of the visible spectrum can be neglected as insignificant. The light is very brilliant; it produces about 650 lumen after a brief warming-up period, and will deliver approximately 300 foot-candles at one foot. This illumination is in excess of what is considered adequate. However, visual acuity is little influenced by intensity of illumination within wide limits.[18] An ordinary 25-watt electric bulb served as source of polychromatic light for the control tests, and, by varying the distance of both sources, the amount of reflected light from the visual-acuity chart could be adjusted to two foot-candles for either light.

Method

There were 55 patients, ranging in age from 12 to 56 years and averaging 29 years. Most of them were university students, and excellent coöperation was obtained when subjective tests and discrimination of details were involved. Two drops of 2-percent homatropine and one drop of 1-percent paredrine were used, and the examination started approximately one hour after instillation of the last drop.

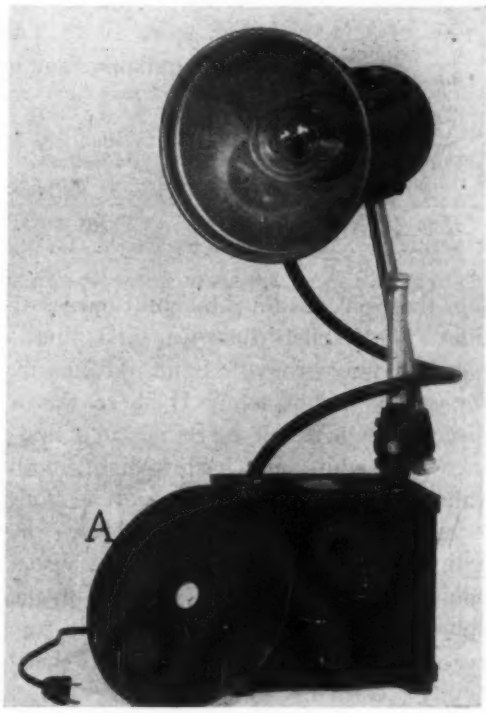

Fig. 1 (Van Wien). The Gates sodium-vapor lamp and the cover (A) used to convert it into a retinoscopy lamp.

1. Retinoscopy was performed with sodium light, and the procedure repeated with polychromatic light. The exact distance of one meter was marked off to eliminate any possible discrepancy in find-

ings due to an error introduced by performing the retinoscopy at different distances. No attempt was made to determine the point of neutralization, but the first lens that would reverse the movement of the shadow was noted. A plain mirror served as retinoscope.

2. The test was performed by deducting one diopter from the retinoscopic findings that were obtained by both sources of light. The Snellen chart was first illuminated by polychromatic light and then by the sodium-vapor lamp. If there was a discrepancy between the retinoscopic findings for white and yellow light, both values were used with both sources of illumination. No change was made in the cylindrical correction but, if the visual acuity could be improved, changes in the spherical values were made, and the correction that would give the best visual acuity recorded.

3. In every instance, an attempt was made to determine the "punctum proximum," that is, the closest distance at which the smallest print could be read. If possible at all, the same size print was used for yellow and ordinary light. Quite frequently, however, a smaller size print could be read at a closer distance with one source of light than a larger size at a farther distance with the other. In this way, the determined values were still of a qualitative, though not quantitative, significance. The distance correction that gave the best visual acuity was worn for this test.

4. The postcycloplegic test was performed 5 to 8 days later. First, white light was used, and every effort made to obtain the best possible visual acuity. Only then was it determined whether there was the same, better, or poorer vision with sodium light. Again, every effort was made to improve the vision by changes in the spherical correction.

TABLE 1

RETINOSCOPIC FINDINGS FOR SODIUM AND POLYCHROMATIC LIGHT

+¼D. More With Polychrom. Light	+¼D. More With Polychrom. Light	Identical Findings	+¼D. More With Sodium Light	+¼D. More With Sodium Light	Total
5 (4.5%)	29 (26.4%)	72 (65.5%)	3 (2.7%)	1 (0.9%)	110 (100.0%)

5. The punctum proximum was determined for white and yellow (the distance correction was worn by the patient for this test).

It appeared more appropriate to evaluate the objective results according to individual eyes rather than patients because, in most instances, there was a difference between both eyes.

The retinoscopic findings, both for polychromatic and sodium light, were almost identical. The slight differences are tabulated in Table 1.

The subjective results—both visual acuity and preference for either form of illumination—depend to some extent on the judgment of the patient. Allowance should be made for some uncertainty in discriminating small details when dealing with untrained observers. Of the group, 70 percent gave excellent coöperation; 14 percent were hesitant but did not contradict themselves; and 16 percent contradicted themselves more than once, but did not have to be excluded as unsatisfactory. Of the total of 55 patients, six did not return for a postcycloplegic test. Thus, complete data are available for 49

cases concerning the subjective test under both cycloplegic and postcycloplegic examination.

Results

In presenting the results for the near test it must be considered that their value under cycloplegia is open to criticism. It was reasonable to expect that with the eyes under the influence of cycloplegia, one would be unable to read even large print at a rather short distance. Therefore, it was surprising to note that most patients were able to read relatively small print at a fairly close range. Possibly the strength and amount of homatropine used was insufficient to effect complete cycloplegia. Nevertheless, although there was some residual accommodation left, the figures were, at least, of relative value, inasmuch as there was considerable interference with the accommodation. Only a small number could not be tested at all because the cycloplegia was so complete that they were unable to read even the largest print of the near test chart at closer than 40 inches under either form of illumination. Five patients were excluded because their answers varied—possibly due to a clonus of the ciliary muscle. The data for the remaining 28 subjects were as follows: The "near point" was identical for nine of them under both forms of illumination, slightly closer for two under sodium light, and definitely closer for 12 under white illumination. For the determination of the actual near point during the postcycloplegic test, patients requiring presbyopic correction were excluded, leaving a total of 44 cases. The near point for white and sodium light was identical for 41 of these and only slightly closer under white illumination for three.

TABLE 2

SUBJECTIVE PREFERENCE AND VISUAL ACUITY FOR CYCLOPLEGIC AND POSTCYCLOPLEGIC TESTS

	Subjective Preference	*Better Visual Acuity
White for cycloplegia and postcycloplegia	0	0
Sodium light for cycloplegia and postcycloplegia	21	6
White for cycloplegia, Sodium light for postcycloplegia	2	0
Sodium light for cycloplegia, White for postcycloplegia	3	0
No preference for cycloplegia, Sodium light for postcycloplegia	5	3
No preference for cycloplegia, White for postcycloplegia	5	3
Sodium light for cycloplegia, No preference for postcycloplegia	8	5
White for cycloplegia, No preference for postcycloplegia	1	1
No difference for cycloplegia or postcycloplegia	4	31
Total	49	49

* Visual acuity was considered "better" if one or both eyes could see at least four additional letters.

Comment

According to all investigators of the subject, there seem to be definite advantages in the use of sodium light for ophthalmoscopy. However, the pathologic changes that could be examined most advantageously with this form of illumination were minute, and could be seen with much greater ease in direct ophthalmoscopy. The sodium lamp, in its present form, is well adapted as a source of light for indirect ophthalmoscopy. In direct ophthalmoscopy, the self-illuminating ophthalmoscope has so many advantages that it seems doubtful whether ophthalmologists, even to obtain added information about minor details, could be induced to resort to the rather cumbersome tech-

nique of using reflected light. It is obviously impossible to incorporate a sodium lamp into the head of the customary hand ophthalmoscope. To incorporate a sodium lamp into a Gullstrand type of binocular ophthalmoscope does not present insurmountable difficulties, but would add another costly piece of equipment to the already vast instrumentarium of the oculist. The relatively few advantages that can be expected hardly justify the recommendation of such an instrument, even for large clinics.

The sodium lamp is an ideal source of monochromatic light since for all practical purposes it emits only the D1 line of 5,897 and D2 line of 5,891 A. U. It is also within the fraction of the spectrum that is reflected from the choroid. So it is not surprising that it was chosen as a very convenient and eminently practical source. Still, other forms of monochromatic light would have been just as suitable. It could be argued that thallium, with its single emission line in the green part, would be just as satisfactory. There are other emission spectra (especially if used with filters) that could be mentioned.

Retinoscopy, if performed with monochromatic light, of necessity requires that exact wave length for which the eye supposedly is focused. Sodium light fulfills this prerequisite as we know it and should, therefore, be the ideal source of light for retinoscopy if any advantage is obtainable from use of monochromatic light.

No different results could be expected from those obtainable with polychromatic light but it was anticipated that the point of neutralization or reversal would be more distinct with sodium light. This expectation, in the author's experience, did not materialize—an unexpected and entirely disappointing result.

On the contrary, retinoscopy with polychromatic light was just as distinct, and no advantage whatsoever could be discovered by using sodium light. As indicated in Table 1 results were identical in 65.5 percent of the cases. In 31.0 percent of the cases, there was a tendency towards the positive side with white light, but in 26.4 percent, this difference amounted to only ¼ diopter, and to ½ diopter in only 4.5 percent of the cases. In 3.6 percent, the findings tended toward the positive side with yellow light, the difference amounting to ¼ diopter in 2.7 percent. Although precautions were taken to perform the retinoscopy at exactly one meter, a difference of ¼ diopter was still considered within the limits of possible error. This leaves only six cases (5.4 percent) with a difference of ½ diopter—a surprisingly small number. Of 38 eyes that showed variations, 27 (24.5 percent) accepted the findings obtained with white light, 11 (10.0 percent) those for sodium light. In other words, if any conclusions could be drawn at all, findings with polychromatic light were slightly more accurate.

For the postcycloplegic test, this tendency was slightly reversed to favor sodium light. It was interesting to note that quite a number of patients subjectively preferred sodium light. This might have been partly because the contours are somewhat softer with the latter, partly because the patients, although unaware of the purpose of the examination, were overly eager to coöperate, and decided in favor of the novel and unusual form of examination.

Of the 49 cases with complete data for cycloplegic and postcycloplegic tests, 21 (42.9 percent) expressed preference for sodium light on both occasions. This contrasts with six patients (12.3 percent) who actually showed better visual acuity. None of them expressed preference—or showed increased visual acuity—for

polychromatic light on both occasions. The 31 (63.3 percent) who showed no actual difference in visual acuity, contrast with 21 (42.9 percent) who, subjectively, preferred sodium light and four (8.2 percent) with no subjective preference for either light during cycloplegic and post-cycloplegic tests. The remainder of the results in Table 2 are within such limits as can be expected from an investigation of this kind, and, consequently, require no further comment.

The question as to whether there is a selective accommodation for a specific portion of the spectrum is quite involved, and cannot be answered by conclusions that are based on only one particular wave length. However, it is felt, if such a phenomenon actually exists, the findings, even for this one particular wave length, would demonstrate such a tendency. No such tendency existed with the accommodative mechanism intact.

Of 44 cases, 41 (93.2 percent) had the identical near point for white and yellow. However, of 28 patients whose accommodation was paralyzed (or at least greatly impaired) by the cycloplegic, 12 (42.85 percent) showed a definitely closer "near point." This is more than a coincidence, and is regarded as additional proof for the actual existence of "paradoxical accommodation."

A number of patients whose visual acuity was less than normal, were tested with white and yellow light. Some of these patients had only refractive errors. In others, the vision was actually impaired by opacities of the media. In all of these, the visual acuity was better with sodium than with polychromatic light. It is reasonable to assume that the improvement was due to the elimination of the chromatic aberration. This is an analogy to the improvement of vision by means of a stenopaic disc, and to the elimination of spheric aberration. Possibly, this may explain why a small number of patients actually had better vision with sodium light, namely, there may have been a slight error in their refraction, which if corrected, would have caused identical visual acuity for white and yellow.

Just as much as spheric aberration is not corrected by the wearing of stenopaic spectacles, sodium lighting is not the answer to the elimination of chromatic aberration. So far as these investigations indicate, no advantage is obtained through the use of the sodium lamp for interior illumination; where improved visual acuity has resulted from installations of this nature, it is believed that closer investigation would have disclosed errors of refraction which if corrected would have provided equal visual acuity under polychromatic illumination.

Summary

1. Certain advantages for funduscopy with sodium light reported by previous investigators are enumerated. These advantages are due to the greater penetrating properties of monochromatic light.

2. Results of retinoscopy, both with sodium and polychromatic light have been compared. No essential difference was encountered, and no advantages could be discovered in favor of sodium light.

3. With proper corrections, no increased visual acuity could be observed with sodium light.

4. With the ciliary mechanism intact, no evidence was noted that there is selective accommodation for the yellow portion of the spectrum.

5. Under cycloplegia, print can be read at closer distance with white light, and this may be additional proof for the so-called "paradoxical accommodation."

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References

[1] Mayou, T. O. S. Cited by Duke-Elder, W. S. Textbook of Ophthalmology. St. Louis, C. V. Mosby Co., 1938, v. 2, p. 1176.

[2] Vogt, Alfred. Ophthalmoskopische Untersuchungen der Macula lutea im rotfreien Licht. Klin. M. f. Augenh., 1921, v. 66, p. 321.

[3] Friedenwald, Jonas S. Freely movable instrument for ophthalmoscopy with yellow-green light. Amer. Jour. Ophth., 1924, v. 7, p. 940.

[4] Cousin, G., Monnier, Alfred, and Mouton, Marcel. Sur l'emploi d'une lumiere sélective pour réduire l'eblouissement. Société Française d'Ophthalmologie. Bulletins et Mémoires, 1934, v. 47, p. 62.

[5] Bichelonne, Favory, and Bégué. Emploi de la lumiere jaune sélective en Ophthalmologie. Société Française d'Ophthalmologie. Bulletins et Mémoires, 1935, v. 48, p. 3.

[6] Kleefeld, G. Exploration de l'oeil au moyen de la lampe au sodium. Bulletin de la société d'Ophthalmologie de Paris, 1935, no. 9, Dec., pp. 788-800.

[7] Duke-Elder, W. S. Textbook of Ophthalmology. St. Louis, C. V. Mosby Co., 1938, v. 2, p. 1176.

[8] Koeppe, L. Die Mikroskopie des lebenden Auges. Berlin, Julius Springer, 1922, Bd. 2, p. 113.

[9] Cited by Bichelonne, Favory, and Bégué.

[10] Cited by Kleefeld.

[11] Serr, H. Das Monochromatische Licht der Natriumdampflampe als Lichtquelle fuer Augenspiegeluntersuchungen. Arch. f. Ophth., 1937, v. 137, p. 636.

[12] Roggenbau und Werthauer. Klin. M. f. Augenh., 1927, v. 78, p. 762. Cited by Serr.

[13] Ballantyne, A. J. Modern methods in ophthalmoscopy. Trans. Ophth. Soc. United Kingdom, 1937, v. 57, p. 273.

[14] ———. The use of sodium and mercury vapour lamps in ophthalmoscopy. Brit. Jour. Ophth., 1938, v. 22, p. 204.

[15] Glueck, Emil. Clinical experiences with sodium lamp, Ophthalmologica, 1942, v. 103, p. 369.

[16] Duke-Elder, W. S. Textbook of Ophthalmology. St. Louis, C. V. Mosby Co., 1934, v. 1, p. 763.

[17] Pech, J. L. La Valeur Physiologique et Clinique des Aberrations chromatiques de l'oeil. Arch. d'Ophth., 1930, v. 47, pp. 363-377.

[18] Cowan, Alfred. Refraction of the Eye. Philadelphia, Lea & Febiger, 1938, pp. 148-149.

INTRAEPITHELIAL EPITHELIOMA OF THE CORNEA AND CONJUNCTIVA (BOWEN'S DISEASE)*

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The clinical and pathologic entity on which the condition known as intraepithelial epithelioma is based was first described in two cases of chronic skin tumor by the dermatologist, Bowen,[1] in 1912, as a precancerous dermatosis. Since then, many reports of similar lesions in both skin and mucous membrane have appeared, and the condition has come to be known as Bowen's disease. In 1939, Stout[2] wrote an excellent summary of the cases in the dermatologic literature and, in 1940, Cippollaro and Foster[3] similarly reviewed the reported cases of mucosal lesions.

It remained for McGavic[4] to recognize this condition in tumors of the cornea and conjunctiva and, in 1942, he published a report of five cases with clinical and gross and microscopic studies. The characteristic lesion on cornea and conjunctiva which he described consists of "slightly elevated, diffuse, sometimes multiple, highly vascular patches of reddish-gray gelatinous tissue—which arise from epithelium and may remain entirely within the epithelium for years without breaking through the basement membrane to show the usual tendency of epitheliomas to invade or metastasize."

Microscopically, these tumors showed loss of an orderly arrangement of the epithelial cells, which were hyperchromatic and variable in size with mitotic figures and giant cells containing either clumped nuclei (Bowen cells) or a single giant nucleus; intact basement membrane, and a degree of inflammatory reaction in the submucosa.

Complete surgical excision was given as the treatment of choice, and radiotherapy was quoted as being contraindicated in the opinion of some pathologists, but McGavic did dwell on the difficulties of complete excision short of enucleation where the conjunctiva is also involved.

A sixth case was reported by George Wise,[5] in 1943.

A seventh case of Bowen's tumor of the conjunctiva was reported by Khanolkar,[6] in 1946. Repeated excision resulted in recurrences, of which the last showed malignant changes. Radium application was followed by no recurrence for the remaining four years of this patient's life.

CASE REPORT

P. G., a 63-year-old Puerto Rican woman, was admitted to the Eye Clinic of the Manhattan Eye, Ear, and Throat Hospital, service of Dr. R. T. Paton, on May 21, 1946, with a history of growth on the right eye of five months' duration. There was no previous history of ocular injury or inflammation.

Eye examination. The left eye was normal, with clear media and negative findings for the fundus. Visual acuity was 20/40 with the illiterate chart, due principally to poor coöperation. The right eye showed a visual acuity of 10/200, which could not be improved. The bulbar conjunctiva was slightly injected. In the lower nasal quadrant of the cornea and crossing the limbus was a mass (fig. 1), about 5 mm. in diameter and elevated

* From the Eye Department (Service of Dr. R. T. Paton) and the Radiotherapy Department of the Manhattan Eye, Ear and Throat Hospital. Read before the New York Society for Clinical Ophthalmology, February 3, 1947.

about 1 mm. It was pinkish gray in color, with a slightly granular surface and the texture of a cauliflower. In the surrounding cornea, including the pupillary area, there was a faint grayish infiltrate, and the bulbar conjunctiva and episclera immediately adjacent to the tumor were

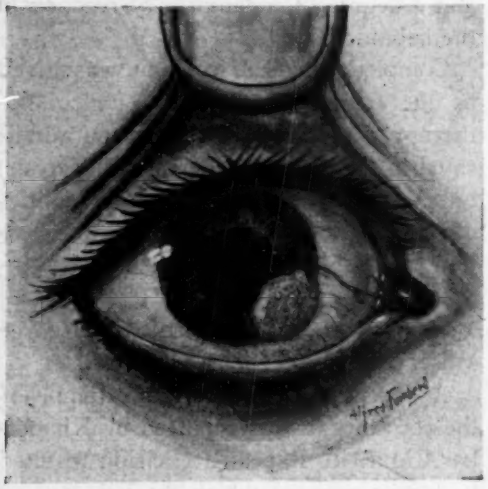

Fig. 1 (Esterman, Laval, and Okrainetz). Intraepithelial epithelioma of the right cornea and conjunctiva before radiation.

more congested than the remainder of the eye. There were no keratic precipitates, cells, or flare. Ocular tension was soft. Dilation of the pupil revealed a faint, posterior, cortical lens opacity and a clear vitreous. The fundus was not perfectly visualized, but there was no gross pathologic condition. There were no palpable regional lymph nodes.

Physical examination. The general physical examination was essentially negative except for a soft systolic murmur at the cardiac apex; and slight transverse cardiac enlargement; blood pressure was 144/86 mm. Hg, urine was normal, Wassermann and Kahn tests were negative, blood sugar was 125; X-ray studies of skull, lungs, and long bones showed no evidence of tumor or erosion.

Laboratory report. On May 23, 1946, a portion of the tumor was excised for biopsy. The report by Dr. Joseph Laval follows:

"The low power (fig. 2) shows proliferation of the epithelial cells without any involvement of the corneal stroma or any other ocular layers. There is no inflammatory reaction and no hemorrhagic factor. The mass has a fairly well-defined external limiting surface with no evidence of necrosis or secondary infection. The high power (fig. 3) shows the basement membrane well defined, with no break through of any of the epithelial cells. Occasional mitosis is present. There are no pearl formations, or evidence of keratinization. No giant cells are seen and no so-called "monster cells" are present. The picture is typical of Bowen's intra-

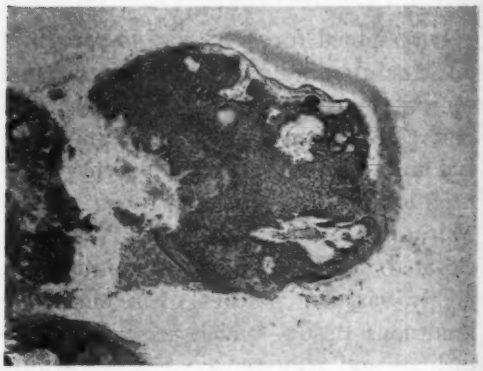

Fig. 2 (Esterman, Laval, and Okrainetz). Low-power photomicrograph of biopsy; intraepithelial epithelioma of right cornea.

epithelial tumor in all respects except that no monster cells were found. I do not know whether the absence of monster cells is enough to throw out the diagnosis of Bowen's tumor of the cornea, but because the remainder of the picture is typical, I am inclined to consider this case one of Bowen's tumor."

Treatment. Since the tumor involved conjunctiva as well as cornea, it was de-

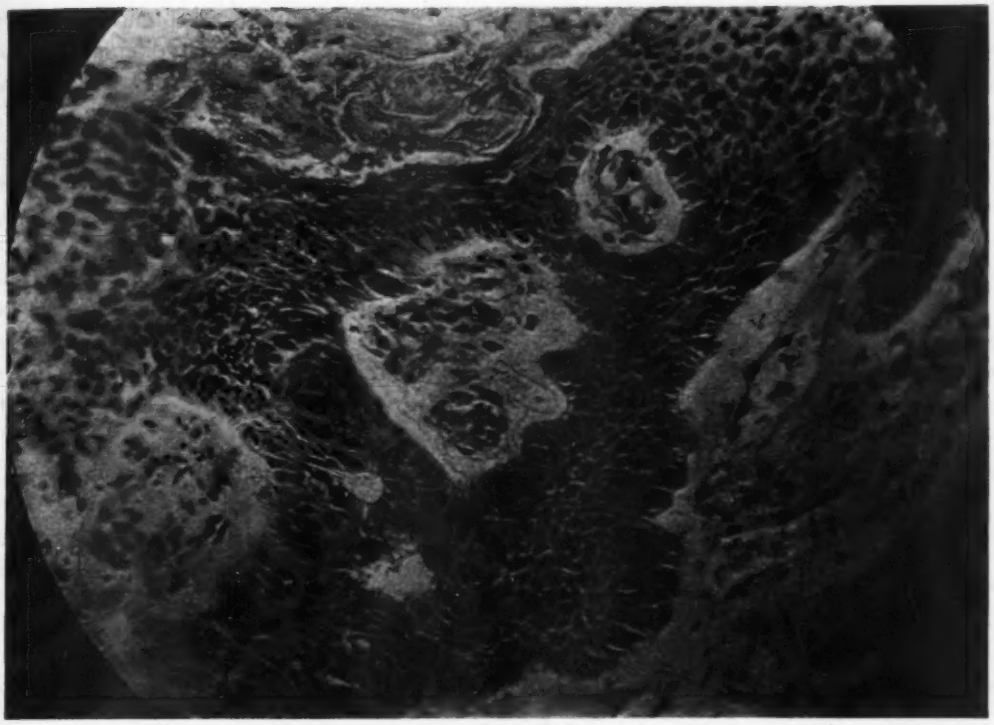

Fig. 3 (Esterman, Laval, and Okrainetz). High-power photomicrograph of biopsy: intraepithelial epithelioma of right cornea.

cided to attempt radiation. Accordingly, beginning May 29, 1946, under the direction of Dr. Okrainetz, the patient received nine treatments of low voltage unfiltered X-ray therapy in fractionated doses of 600r. every other day for a total of 5,400r. in 18 days. Under pontocaine anesthesia the lesion was screened off with lead foil leaving an exposed area of 1.5 by 1.5 cm. Using 60 K.V.; 5 Ma.; no filtration; target skin distance 10 cm.; H.V.L.: A1-0.4 mm.; output 610r. per minute, each treatment lasted 1½ minutes.

During the course of therapy, the patient had moderate hyperemia of the bulbar conjunctiva and slight pain which was promptly relieved by boric-acid ointment. After a few exposures, the lesion became thinner and at the end of the course of treatments the tumor had entirely disappeared.

Results. On July 30, 1946, six weeks after completion of radiotherapy, the right eye was white except for a barely perceptible injection of the bulbar conjunctiva in the lower nasal segment of the globe. The tumor mass on both the cornea and the conjunctiva had melted away completely (fig. 4) leaving only the faint infiltrate previously seen and a few small deep vessels originating from the limbus. On the surface of the cornea, at the site of the growth, there remained a very shallow depression, 0.5 mm. at its deepest point.

Dilation of the pupil revealed no increase in the lens opacity noted prior to radiation. Ocular tension had remained soft. Visual acuity was unchanged.

Fig. 4 (Esterman, Laval, and Okrainetz). Reproduced from a Kodachrome of the right eye taken after completion of the radiotherapy.

In November, 1946, the condition was unaltered, except for a slight increase in superficial vascularization originating from the limbal vessels at the tumor site, resembling a pseudopterygium. The most recent examination (September, 1947) shows this condition to have remained substantially the same, with no lens changes.

Conclusion

This case will, of course, require a longer follow-up period before any conclusions can be drawn as to the efficacy of radiotherapy. It is presented with the thought that it may stimulate others to be on the watch for this type of tumor, which otherwise might be considered basal- or squamous-cell carcinoma, papilloma, or simple hyperplasia; and that, if this form of therapy should prove successful, it may provide a more effective method for treating this type of growth in which there is involvement of the conjunctiva as well as the cornea.

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References

[1] Bowen, J. T. Precancerous dermatosis. Jour. Cutan. Dis., 1912, v. 30, May, p. 214.
[2] Stout, A. P. Malignant manifestations of Bowen's disease. N. Y. State Jour. Med., 1939, v. 39, April 15, p. 801.
[3] Cipollaro, A. C., and Foster, P. Bowen's precancerous dermatosis of mucosa. N. Y. State Jour. Med. 1940, Feb. 15, v. 40, p. 246.
[4] McGavic, J. S. Intraepithelial epithelioma of the cornea and conjunctiva. Amer. Jour. Ophth., 1942, v. 25, Feb., p. 167.
[5] Wise, Geo. A case of Bowen's disease. Amer. Jour. Ophth., 1943, v. 26, Feb., p. 167.
[6] Khanolkar, V. R. Bowen's disease of the conjunctiva. Amer. Jour. Ophth., 1946, v. 29, May, p. 515.

OCULAR CHANGES IN ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS*

Report of a case with microscopic findings

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A report of the microscopic findings in the retina, choroid, and optic nerve of a case of acute disseminated lupus erythematosus in which the fundus lesions were observed clinically is sufficiently rare to warrant publication.

As Klauder and De Long[1] point out, lupus erythematosus is an exceedingly rare, chronic, less commonly acute, inflammatory disease of the skin. It is characterized by sharply marginated, red or violaceous, variously sized patches. The lesions are found on the face much more commonly than elsewhere. These patches are followed by cicatricial atrophy.

The following clinical varieties have been described: (1) A circumscribed or discoid form; (2) a chronic variety; (3) a diffuse or disseminated variety which may be acute and terminate fatally; (4) a telangiectatic variety; (5) a nodular type.

In the great majority of cases the disease makes its appearance in the chronic discoid form. In this report we are concerned only with the rare Type 3, which is an acute or subacute, often recurrent, type marked at times by widely disseminated polymorphic lesions of the skin and mucous membranes, accompanied by constitutional symptoms. Frequently there is a widespread visceral involvement and a variable clinical picture. As Kierland[2] pointed out, the Senear-Usher and the Libman-Sacks syndromes are related to this condition. Although some internists and dermatologists believe that the localized discoid type of lupus erythematosus is a different disease from acute disseminated lupus erythematosus, it is significant that in a third of a series of 30 cases of acute disseminated lupus, Montgomery[3] found that the disease started as the chronic localized discoid type. The interest of internists in disseminated lupus erythematosus, according to Stickney,[4] dates from a paper by Osler,[5] in 1895, on the "erythema group" in which he emphasized the grave systemic manifestations of a group of cases, many of which were undoubtedly disseminated lupus erythematosus. Since the disease is entirely distinct from lupus vulgaris, and since a tuberculous etiology has not been proved, Rose and Pillsbury[6] feel that it is unfortunate that the term "lupus" is part of the nomenclature of the disease.

General manifestations of the disease

While the disease is rare, Ludy and Corson[7] state that acute disseminated lupus erythematosus is rapidly increasing in frequency. The disease has been studied extensively by Stillians,[8] Matthews,[9] Rose and Pillsbury,[6] Stickney,[4] and others.

In addition to the skin lesions the symptoms are those of a prolonged low-grade fever which fluctuates irregularly.

The skin lesions may precede, accompany, or follow the visceral and systemic manifestations of the disease, or they may

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† By invitation.

be entirely absent. As a rule they are polymorphic and active. The exposed surfaces of the body are the sites of predilection, although no cutaneous or mucous surface of the body is exempt. A wide variety of lesions may occur simultaneously or in succession such as urticarial, eczematoid or erysipeloid areas, purpura, petechiae, purplish or reddish brown macules, bullae, telangiectasis, and ulcers. The most common lesion is the deeply erythematous, swollen patch or plaque of varying size. In acute disseminated lupus erythematosus, a puffy erythematous lesion may appear upon the face, and include a goodly portion of it. There may, for a time, be a sharp demarcation about the eyes and at the frontal hairline, but the eruption soon becomes disseminated and involves large portions of the extremities and trunk. Hemorrhagic, vesicular, and bullous lesions are numerous. When remissions occur, marked atrophy, scarring, or pigmentation may follow subsidence of the acute lesion. Deep subcutaneous abscesses are not infrequently observed. The lesions may resemble a number of cutaneous diseases, such as seborrheic dermatitis, dermatitis venenata, erythema multiforme, Boeck's sarcoid, erysipelas, pellagra, and others.

There is gross evidence of pathologic changes in the endocardium in 30 percent to 50 percent of the cases. The tricuspid and mitral valves are most frequently involved, and show nonbacterial vegetations on the endocardial surfaces. Even though the lesions occur chiefly in the endocardium and pericardium, electrocardiographic examination may show some damage to the myocardium. Acute lupus erythematosus may simulate bacterial endocarditis or acute rheumatic fever; however, the cultures are negative.

Renal involvement occurs in practically every case. The clinical picture may suggest glomerulonephritis, pyonephrosis or nephrosis, "diffuse" or "interstitial" nephritis, or tubular nephrosis. Urinary findings are not consistently characteristic of any particular type of renal lesion. Baehr, Klemperer, and Schifrin[10] have described what they believe to be the characteristic renal lesion of the disease, and one which they report having seen in no other condition, with the possible exception of the kidney of eclampsia. This renal lesion consists of a peculiar hyaline thickening (wire loop) of the walls of the glomerular capillaries. These wire loops have been found to contain no amyloid or lipoid material. Accompanying these changes they describe proliferative and thrombotic processes involving part or all of the glomerular vasculature; the picture may resemble that of the embolic glomerulonephritis seen in subacute bacterial endocarditis. Renal involvement has been considered the most common visceral manifestation. Renal insufficiency, however, does not play an important role in causing death, since, as Keith[11] points out, severe chronic uremia very seldom occurs.

Patients with this disease also show a leukopenia, anemia, loss of weight, and asthenia, followed by marasmus and cachexia. Stillians[8] pointed out that the white-cell count may be at a low normal level, and that it fails to rise with elevation of the temperature. When positive blood cultures are obtained, Matthews[9] feels they are the result of contamination, or are due to a terminal bacteremic invasion by organisms having no causal relationship to the disease.

Lymphadenopathy may be generalized or localized to the cervical region. Both the superficial and deep lymphatic chains may be affected. Enlargement is usually moderate but occasionally glands as large as a fist may be observed. Matthews[9] found nothing characteristic about these glands in microscopic sections.

It is interesting that Matthews[9] found the serologic tests for syphilis falsely positive in 17 percent of the cases. The sedimentation is also frequently found to be increased in rate.

Hepatomegalia has been reported as a common finding and is said to result from cloudy swelling, pylephlebitis, or abscess formation. Jaundice may occur but is rather infrequent. Splenomegalia occurs rather frequently but it rarely attains an extreme degree. The splenic enlargement, according to Matthews,[9] is usually due to infarction. Rose and Pillsbury[6] have demonstrated that the spleen may show parenchymatous degeneration, acute splenitis and perisplenitis, acute congestion, necrosis with arteriolar obliteration, abscess formation, and infarction.

In the gastrointestinal tract, embolic and thrombotic phenomena occur in the mesenteric circulation and this may result in a picture simulating acute abdominal emergencies and lead to unnecessary surgical exploration. Hematemesis and melena are frequent manifestations of ulcerating lesions in the mucosa of the stomach or intestines. Diarrhea is the commonest gastrointestinal symptom.

This disease also affects the lungs; in fact pulmonary involvement is among the chief causes of death. The lesions found clinically and at autopsy are variable and include pneumonia, abscess formation, gangrene, atelectasis, and infarction. Pleural effusions are common and may be serous, sanguineous, or purulent. Severe tracheolaryngitis has been seen occasionally.

The disease seems to have a predilection for the larger joints, and synovial effusions of a serous, sanguineous, or purulent character may occur. The joint symptoms may resemble those of fibrositis, rheumatic fever, and acute, subacute, or chronic infectious arthritis. Rose and Pillsbury[6] also point out that arthralgia may precede or accompany the eruption and systemic phases of the disease.

The mucous membranes may also be involved and ulcerative lesions may occur in the gastrointestinal tract, vagina, bladder, and pharynx, which give rise to alarming hemorrhages. Matthews[9] reported gangrenous ulcerations in the mouth, tonsils, and pharynx.

As a result of central nervous-system involvement, convulsions may occur even in the absence of renal disease and uremia. The colloidal gold curve may be of the paretic type. Careful pathologic studies of the brain have revealed vascular changes in many instances.

The disease is found in all age groups, but women between puberty and the menopause are in the large majority. In Kierland's[2] cases, they were predominantly in the 20- to 30-years age group. He also found that 80 percent of the cases having the subacute and acute form of this disease occurred in women. These figures are in agreement with those of other observers.

Etiology

The etiology of acute disseminated lupus erythematosus is essentially unknown but several possible causative factors have been suggested. Inasmuch as there is a close association with tuberculosis in many of the chronic cases of lupus erythematosus, it has received a good deal of serious consideration as a causative factor. This association is not so evident in the acute form of the disease. According to Stillians,[8] associated skin lesions of lupus erythematosus never give histologic evidence of tuberculosis. Other writers regard the disease as a manifestation of tuberculous infection or as an allergic response to tuberculo-toxin; this view appears to be based largely upon the following facts: (1) The oc-

casional occurrence of active tuberculous lesions in patients with the disease; (2) the alleged recovery of tubercle bacilli from the blood stream in some cases; and (3) the marked response which usually occurs after tuberculin inoculation. Slocumb[12] has stated that the incidence of tuberculosis in American patients with lupus erythematosus is no greater than that found in any other systemic disease. Bergmeister[13] and Pillat,[14] respectively, have classified the intraocular lesions as metastatic tubercles in the retina and as acute tuberculous choroiditis. In spite of the above facts and the implications suggested by its name, lupus erythematosus is no longer considered to be of tuberculous origin.

Another theory which has received consideration is that the disease is the result of a generalized toxic reaction similar to the Shwartzman phenomenon. According to Stillians,[8] Brocq's theory that toxins from infectious foci of various kinds are responsible for the lesions of lupus erythematosus has long been the favorite among dermatologists.

The release of unknown toxic products elaborated in the skin by various physical agents has also been considered as the causative factor. The tendency for acute cutaneous and systemic manifestations to appear or recur after exposure to sun or ultraviolet light, roentgen rays, insect bites, cold, or the intracutaneous injection of irritating substances such as tuberculin has long been known.

Kiel[15] has advanced what he terms the "vascular concept" of the disease. He assumes the presence of a theoretical toxin that has a selective affinity for the vascular system, chiefly the capillaries and to a lesser degree the venules and the arterioles. The action of this toxin produces proliferation of the vascular endothelium with subsequent formation of thrombic, perivascular hemorrhages and edema. These lesions are found in every structure of the body but occur chiefly in the skin, joints, lymph nodes, bone marrow, lungs, heart, and spleen. Wagener,[16] however, doubts that the type of retinopathy found in this disease is of vascular origin and feels there is a lack of histologic evidence to support the theory.

Stokes, Beerman, and Ingraham[17] advance the hypothesis of an infection-allergy being the causative factor. They conclude that as the discoid type of lesion is expressive of local cutaneous infection-allergy of the follicular inflammatory type, so the acute disseminate type is the clinical type of lupus erythematosus with multiform disseminated cutaneous and systemic lesions resulting from allergic inflammation of the vascular system. The vasculo-allergic type then may be preponderantly local and cutaneous in its manifestations or preponderantly systemic. They admit that the clinical case for infection-allergy is not "massively pro, though there is also little con." As to the nature of the infection to which allergy develops or exists, they admitted that no absolute decision could be "had at this time."

Diagnosis

The diagnosis of lupus erythematosus in the present state of our knowledge of the disease must depend chiefly, as Montgomery[3] has pointed out, on the recognition of the cutaneous lesions. It is recognized, however, that acutely ill patients will be seen who present most, if not all, of the systemic signs and symptoms outlined above, but in whom no cutaneous lesions occur. The various manifestations of acute disseminated lupus erythematosus are not fully understood. All the clinical findings have not been satisfactorily correlated and so the diagnosis is frequently subject to some question. In the differential diagnosis of acute disseminated lupus erythematosus

several conditions must be considered. In *chronic discoid lupus erythematosus* the cutaneous lesions are similiar but there are no systemic manifestations of the disease. The chronic cutaneous lesions are typified by small, scaly, atrophic patches of pigmented skin on the face. If the skin lesions become more or less confluent and widespread over the body, and there is an absence of systemic manifestations, the condition is called *chronic disseminated lupus erythematosus.* Cases of chronic lupus, either the discoid or the disseminated type, according to Klauder and Ellis,[24] may develop into the acute disseminated form with fatal termination.

The ophthalmoscopic picture seen in Koch and McGuire's case[19] was similiar to that which is seen in periarteritis nodosa and less typically in dermatomyositis. Positive blood cultures are sometimes found in the terminal stages but, as Matthews[9] points out, it should be emphasized that a terminal bacteremia is not uncommon in disseminated lupus and this should not be interpreted as evidence of subacute bacterial endocarditis. The so-called Libman-Sacks syndrome is at times accompanied by skin lesions identical to those of acute disseminated lupus erythematosus. It seems beyond doubt that those cases described by Libman and Sacks with erythematous facial lesions were examples of acute disseminated lupus erythematosus. Rose and Pillsbury[6] feel that whether their other cases represent instances of the same disease without erythematous skin lesions must remain uncertain for the present. Thrombocytopenic purpura may precede, accompany, or follow the syndrome of acute erythematous lupus.

Course of the disease

The clinical course of the acute form of this disease is exceedingly variable. Acute exacerbations and remissions typify the disease. The acute form is usually fatal in from two months to four years. The onset may be abrupt and the course short and stormy with fatal termination in 6 to 8 weeks, while other cases may be characterized by mild systemic reactions and prolonged remissions during which all cutaneous and visceral manifestations disappear. The course may be dramatically unexpected. According to Rose and Pillsbury,[6] a moribund patient may occasionally recover or an extremely mild case suddenly become fulminating and rapidly fatal within a few weeks. Renal failure, bronchopneumonia, toxemia, or terminal bacteremia have been reported as the commonest causes of death. Stillians[8] points out that during the course of the chronic forms of the disease (chronic discoid and chronic disseminated types) fever, albuminuria, bone and joint pains, and malaise are warnings of the onset of an acute exacerbation. The chronic discoid type only rarely exhibits rapid extension or acute visceral dissemination.

Therapy

Treatment is purely supportive. Many drugs and varieties of therapy have been tried and found to be of little or no avail. In view of the fact that acute dissemination may occur following exposure to sunlight, ultraviolet radiation, X-ray therapy, trauma from irritating and stimulating local applications, all of these procedures had best be avoided. Gold and tuberculin are said to be dangerous in the treatment of this condition. Matthews[9] has pointed out that it is perhap better to know what not to do than it is to try a therapeutic regime blindly. Early recognition of the disease and the avoidance of certain dangerous procedures, especially exposure to sun and ultraviolet light, may prevent serious or even fatal exacerbations. O'Leary[20] warns that vaccines and serums provoke more unfavorable reactions than do drugs.

General pathology

Mallory[21] has stated that it is not always possible for the pathologist to make a final diagnosis even in a patient with typical clinical manifestations. Characteristic vascular lesions have been described by Baehr, Klemperer, and Schifrin[10] as consisting of (a) capillary dilatation with extravasation of blood and serum; (b) proliferative endothelial vascular lesions with thrombus formation; (c) degenerative or necrotizing lesions in the walls of capillaries, arterioles, and venules, often with hemorrhage into adjacent tissues. All three processes may be found in the same case and in any part of the vascular tree. Hyaline capillary thrombi are characteristic and wide-spread according to Rose and Pillsbury.[6] Montgomery[3] feels that the pathologic changes noted in the various internal organs are "essentially that of a toxic process, and except possibly for certain vegetative changes in the valves of the heart as described by Gross in Libman-Sacks syndrome and the so-called wire-loop lesions in the capillaries of the kidney, the pathologic changes in the various internal organs are not specific or diagnostic for lupus erythematosus."

Fundus changes

Fuchs[22] has stated that various intraocular changes have been described in cases of acute lupus erythematosus. These include papillitis with irregular white circumscribed areas along the retinal veins, acute or healed areas of disseminated choroiditis, and macular involvement with retinal hemorrhages. For the most part the ocular lesions described in the literature have been limited to the retina and choroid, with a number of instances of optic-nerve involvement. There have been wide discrepancies in previous reports as to the types of lesions found in the various ocular structures.

In those cases where the retina showed involvement, the presence of some form of exudate or hemorrhage was regularly found. Prominently mentioned throughout the literature were cotton-wool patches, although in most instances the authors did not refer to them by that term. Such cotton-wool-like exudates were variously described as: fluffy exudates,[10, 23] soft fluffy exudates,[15] or cloudlike patches.[24] Frequently small exudates were referred to as: small white dots in the macular region,[13] small light-colored spots in the macula,[25] small white lesions lying over the retinal vessels in the macular area,[26] small irregular yellowish-white elevated spots,[23] or small, round, white, elevated lesions situated underneath a retinal vein.[27]

Similarly there was no uniformity in the character of the described hemorrhages. More often than not the hemorrhages were small and frequently were located in the macular area,[19, 23, 24, 26] or near the disc.[23] However, larger hemorrhages were also seen, and Koch and McGuire[19] noted a subhyaloid hemorrhage. Maumenee[23] stated that the distribution of the hemorrhages was not in relation to the white patches, nor to the larger retinal vessels. This finding was consistent with Koch and McGuire's[19] opinion that the hemorrhages were located in relatively avascular areas of the retina, but were, however, in close proximity to the capillaries and to the smaller venules and arterioles, especially the former. Other authors, nevertheless, described them as being perivascular.[6, 10, 15]

A less consistent finding was retinal vascular disease. Some of the vascular changes listed were: hyperemia of the retinal vessels,[23] sclerosis,[24] perivasculitis of the arteries,[28] marked periphlebitis and segmented periphlebitis,[19] and areas of complete replacement fibrosis of veins and arterioles.[19]

Optic-nerve involvement was sometimes seen, although usually in a late stage of the disease. Ophthalmoscopically the following optic-nerve lesions were described: hyperemia of the optic nerve,[13] blurring of the disc margins,[23, 25, 27] papilledema,[6, 23] primary optic atrophy,[19, 28] and postneuritic optic atrophy.[29] In addition, circumpapillary edema[10, 19] was seen.

Areas of retinal atrophy were mentioned,[6, 28] and two authors reported retinal detachment.[6, 9] Retinal[6] and subretinal[9] edema were occasionally present. Pillat[14] found healed tuberculous choroiditic lesions in 16 cases of the chronic form. Three of these cases developed into the acute form, and, of these, two developed "indistinct, slightly elevated, grayish-white or yellowish foci of choroiditis in the posterior part of the fundi." Maumenee[23] found miliary tubercules in one case and choroidal degeneration was observed in one case by Rose and Pillsbury.[6] Koch and McGuire[19] described superficial choroidal, roundish, gray-white exudates and some they believed to be at the level of the choriocapillaris.

Pathologic studies of the eyes in acute disseminated lupus erythematosus are met with only rarely in the literature. Maumenee[23] studied five cases histologically. In all five cases he found cytoid bodies in the retina which corresponded to the yellowish-white to white spots seen in the fundi. In addition, two of his specimens showed papilledema and two showed small hemorrhages in the nerve-fiber layer of the retina. In individual instances he found hyaline degeneration of the intima of the arteries typical of arteriolosclerosis; hyaline degeneration of the intima of the choroidal vessels; serous exudate in the choroid and hemorrhages in the stroma of the choroid. In all five cases he found round-cell infiltration of the choroid as did Semon and Wolff[27] in one case. The latter authors also found partially organized subretinal exudates of inflammatory cells. Goldstein and Wexler[28] described a case with optic atrophy in which they found marked degeneration of the media of the retinal arteries, and areas of retinal atrophy showing replacement fibrosis. Kurz,[26] like Maumenee, found cytoid bodies in the nerve-fiber layer. These corresponded in position to the small white lesions which he had seen, ophthalmoscopically, to lie over the retinal vessels in the macular area. He refers to these cytoid bodies as being in the nature of a varicose hypertrophy or ganglioform degeneration of the nerve fibers. Proliferative endothelial vascular lesions with thrombus formation have not been mentioned in any of the eye reports of this disease. It seems strange that if these vascular changes are a characteristic finding in lupus erythematosus that they do not appear in the retinal vessels.

Case report

Mrs. L. T., aged 30 years, was admitted to the University of California Hospital in the Department of Medicine under the care of Dr. William J. Kerr on November 19, 1941. The following data have been obtained from his records.

History. The patient had been in good health until September, 1940, when she complained of generalized headaches and lower abdominal pain appearing at the time of her menstrual periods. Two months later the lower abdominal pain became constant and was associated with burning on urination. She presented herself for examination by her family physician who, it is said, found albumin and cells in her urine and that her blood pressure was 140 mm. Hg. She was informed that she was suffering from nephritis and was put on a dietary regime. In the following months she became weaker, complaining of costovertebral angle pain, generalized muscular pains, and continued burning on urination. In April, 1941, she developed a severe laryngitis and a "lump" in the left side of her neck associated with fever. There were periods of troublesome palpitation, occurring two or three times daily lasting from 5 to 20 minutes. She had no dyspnea with these attacks.

Four months before admission she developed severe dizzy spells which were unrelated to po-

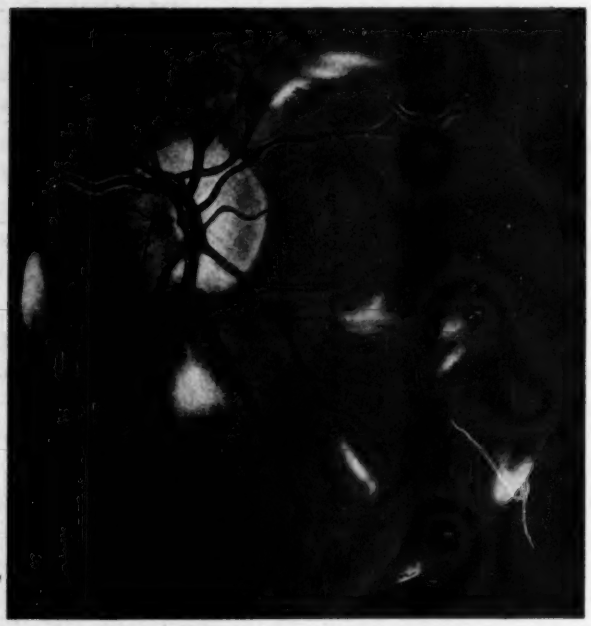

Fig. 1 (Cordes and Aiken). Fundus drawing 5 to 6 months before death, showing questionable or mild edema of nasal margin of the disc, cotton-wool patches, hemorrhages, and vascular changes.

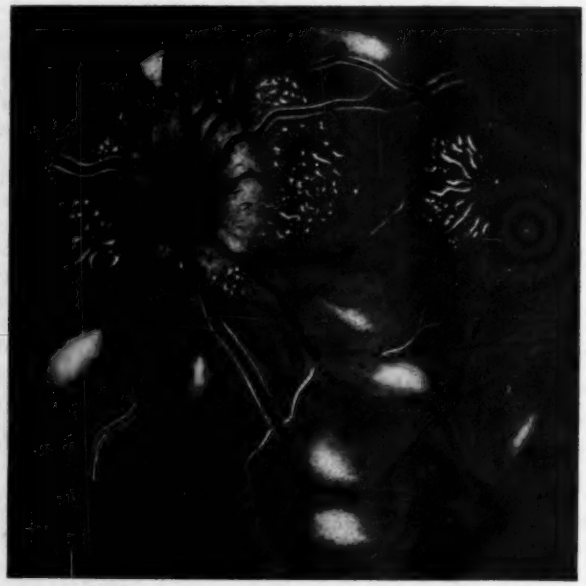

Fig. 2 (Cordes and Aiken). Fundus drawing one month before death, showing edema of the disc, small edema exudates, advanced vascular changes, and evidences of thrombosis of small venous branches.

sition or activity. These dizzy spells usually lasted from 30 to 60 minutes and were associated with nausea. Two months before admission she developed what was called a "staphylococcus enteritis" during which time she vomited and passed numerous diarrheal tarry stools. For 2 or 3 months preceding admission, she ran a daily low-grade fever of around 100°F. On several occasions she developed showers of petechial hemorrhages over her body. She continued to lose weight and strength and when admitted was acutely and critically ill; the temperature was 38.7°C.; pulse 125; blood pressure 180/110 mm. Hg in the right arm, recumbent.

Physical examination. The essential features of the physical examination were moderate dehydration; erythematous macular rash over the cheeks, nose, and chest; evidences of mitral and aortic valvular heart disease; clubbing of the fingers; mild enlargement of the spleen, and a tender nodule, 1.0 cm. in diameter over the left forearm, 5 cm. below the elbow. The mucous membranes were uninvolved.

Laboratory tests showed mild anemia, 3,840,000 R.B.C.; evidences of kidney damage; four negative blood cultures. Spinal fluid colloidal gold, 0000000000; globulin, normal; cell count, 2 W.B.C. and 49 R.B.C.

Course of illness. The patient's general course while in the hospital was one of progressive decline with occasional waves of slight improvement. The blood pressure was generally high but on one occasion was as low as 145/95 mm. Hg, and on another occasion was as high as 210/160 mm. Hg. A low-grade septic type of fever persisted. Substernal and epigastric distress developed. A pericardial friction rub was heard. In addition a pleural friction rub was heard in the left lower axillary region, and pleural fluid was found to be present. The temperature rose steadily, she became comatose, the basis of which was assumed to be a diffuse cerebral vascular lesion. The patient died on June 14, 1942, 20 months after the onset of the disease. Clinical diagnosis at the time of death was acute disseminated lupus erythematosus with Libman-Sacks endocarditis.

Ophthalmoscopic examination. During the six months' hospitalization

period the eyes were examined opthalmoscopically at intervals. There was variable but generally progressive reduction in visual acuity of both eyes. Visual disturbance was most marked and appeared first in the left eye. In the beginning there was questionable or no edema of the discs. Later, edema of the discs was present and persisted to the end. A number of retinal cotton-wool or cotton-wool-like patches (fig. 1) were seen on first examination and were present to greater or lesser amount throughout the period of observation. Retinal hemorrhages were for the most part small and irregular in shape; some were situated in the deeper layers of the retina; others showed striations and were flame-shaped, indicating their location as being in the nerve-fiber layer.

As the edema of the discs increased, it extended a greater distance out into the retina, especially into the macular area where small, irregularly round, white exudates were present (fig. 2). No definite stellate figure developed during the course of the disease.

The most interesting and striking features in the fundi were the vascular changes. The veins were mildly dilated and showed considerable irregularity in caliber. In a number of places they showed perivascular thickening. A shower of hemorrhages was seen along the distribution of several of the small venous branches, indicating the thrombotic nature of the vascular lesions. The spotty and disseminated distribution of the changes in the retinal arterioles was most interesting. In some areas the arterioles appeared relatively normal while in others there were marked irregular localized narrowings, even to the point of complete occlusion. Associated with these narrowings was a varying degree of perivascular thickening. Evidences of arteriolosclerosis were also present. Toward the end the discs began to show pallor.

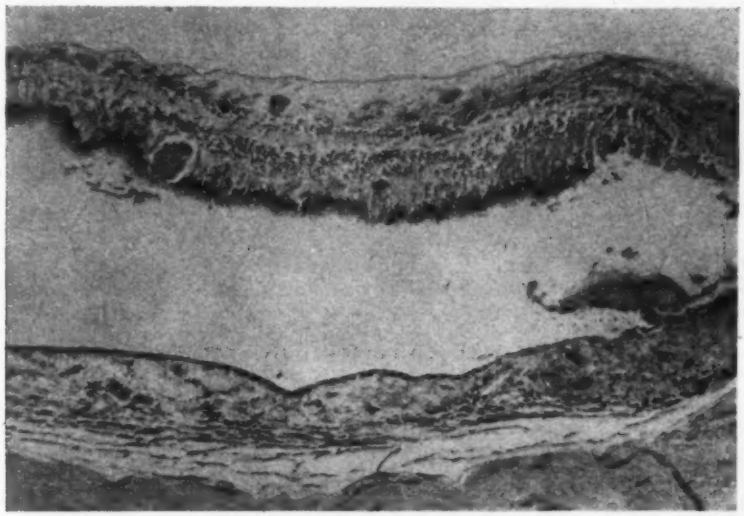

Fig. 3 (Cordes and Aiken). (H&E low power) Retina. There is thrombosis of one retinal arteriole in the section. Also two other retinal arterioles show marked intimal thickening with occlusion of the lumen.

Autopsy findings

General pathologic report (résumé). Mitral and aortic valvulitis; abacterial verrucose vegetations; cardiac hypertrophy. Multiple emboli in the brain stem with areas of focal necrosis involving the inferior portion of the pyramidal decussation. Multiple embolic pulmonary infarcts. Thrombosis of the right auricular appendages. Bilateral bronchopneumonia. Kidneys showed arteriosclerosis and multiple areas of focal glomerulonephritis. There was arteriosclerosis of the heart, spleen, and brain; atherosclerosis of the aorta. Marked central congestion of the liver. Lupus with involvement of the skin of the face and trunk. Right knee showed chronic synovitis.

Eye pathology. (Dr. Michael J. Hogan) *Gross examination.* The specimen consisted of the posterior half of the left eye which was removed at autopsy. Along some of the vessels, which showed white perivascular sheathing, were large, round retinal hemorrhages and a few dense, small round, white exudates. With the dissecting microscope, widespread patchy perivascular sheathing was visible.

Microscopic examination. Retina. Postmortem

changes were fairly marked in all layers, but especially so in the ganglion cell layer, nerve-fiber layer, and in the rod and cone processes. Some of the arterioles showed thrombi, without changes in the structure of the walls and these exudates were found in the outer nuclear layer as well.

Surrounding most of the retinal vessels were fairly broad areas of degeneration (possibly postmortem). These degenerative areas were

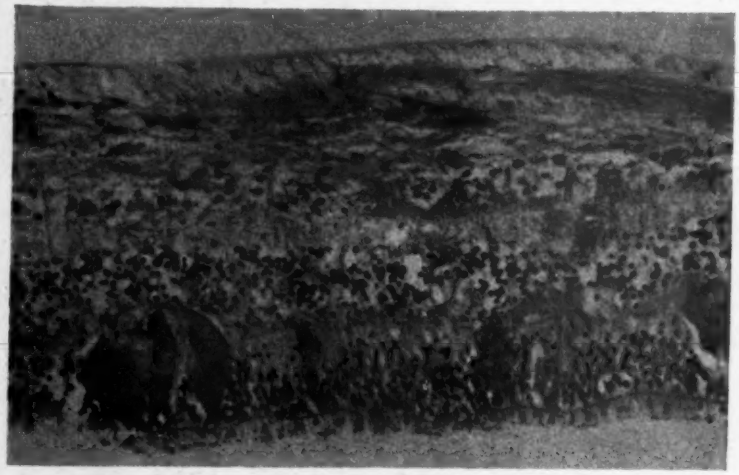

Fig. 4 (Cordes and Aiken). (H&E high power) Retina, showing extensive deposition of the hyalinelike exudate in the outer retinal layers.

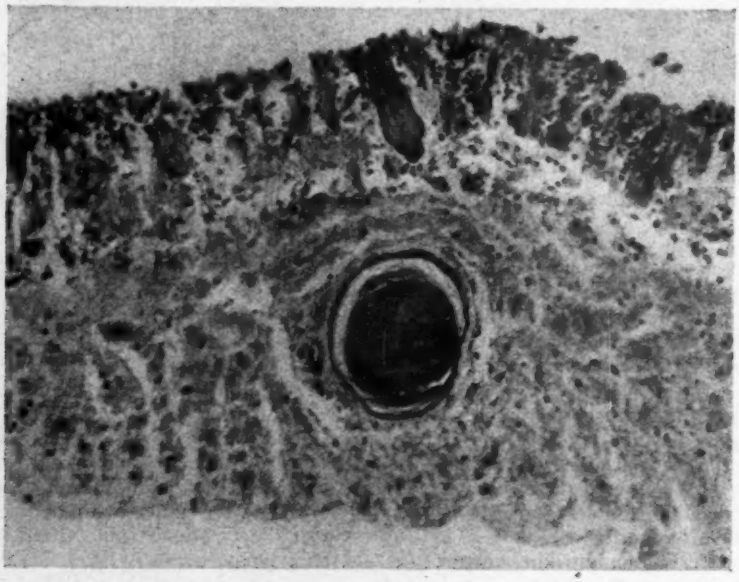

Fig. 5 (Cordes and Aiken). (Verhoeff stain, high power) Retina, showing proliferation of intimal connective tissue, narrowing of the lumen, and thrombosis of a retinal arteriole. Note the retinal exudates in the outer nuclear layer.

were probably embolic in origin (fig. 3). In many sections there were scattered, small, round hemorrhages in the nerve-fiber and internuclear layers, and numerous hyalinelike exudates in all layers of the retina (fig. 4). Near the disc, these also found in the other layers, particularly the internuclear layer. In many sections, the retinal arterioles showed intimal thickening, with narrowing of the lumen (figs. 5 and 6). The smaller arterioles were also similarly affected and at

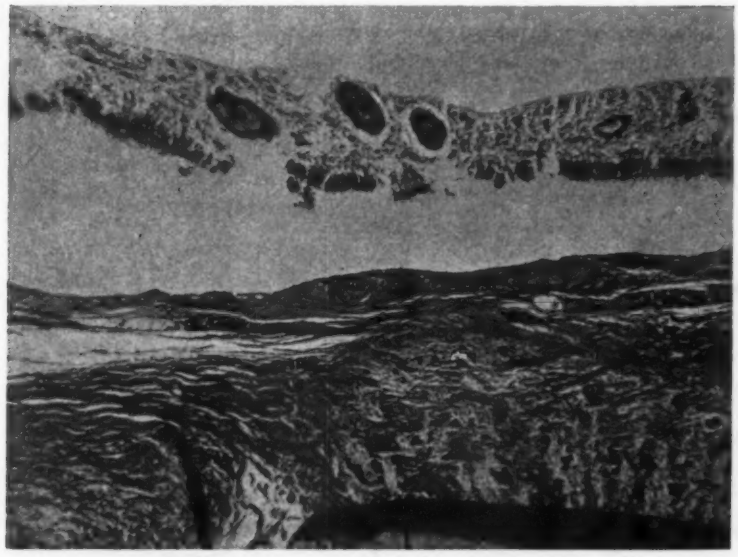

Fig. 6 (Cordes and Aiken). (H&E low power) The retinal vessels near the disc show marked intimal thickening, medial hypertrophy, and extreme narrowing of the lumina with thrombosis. Note the similar changes which have occurred in the small choroidal arteries.

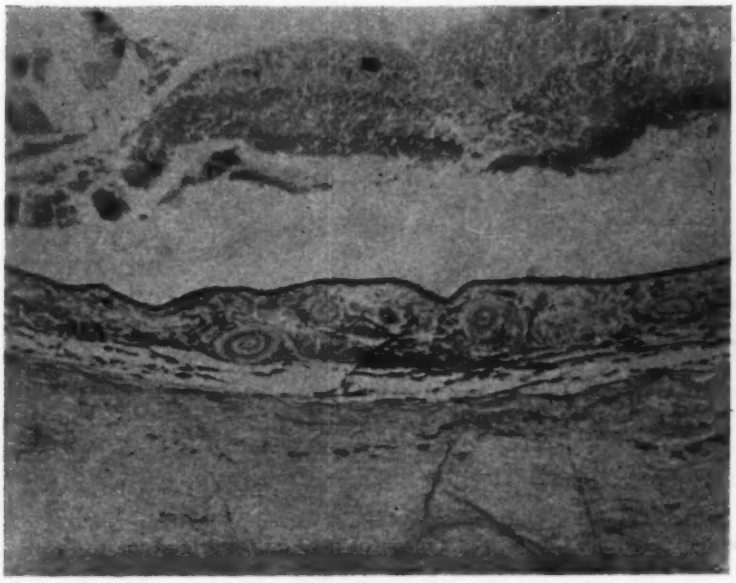

Fig. 7 (Cordes and Aiken). (Verhoeff stain, low power) Choroid. Note the marked narrowing of the lumina of the vessels due to intimal connective-tissue proliferation. One vessel is almost completely occluded.

times thrombosed. Other vessels showed subintimal thickening, with narrowing of the lumen. The veins did not seem to show much involvement. There was no inflammatory infiltration into the retina.

Choroid. The small arteries and arterioles of the choroid showed widespread changes, which were similar to those seen in the retinal arterioles (fig. 7). Some of these vessels showed marked subintimal thickening, and the lumina

were reduced the diameter of 1 or 2 red blood cells, or were completely occluded (figs. 8, 9, 10). Other small arteries contained thrombi without evident disease of the wall. Still others showed marked hyalinization of the walls, with

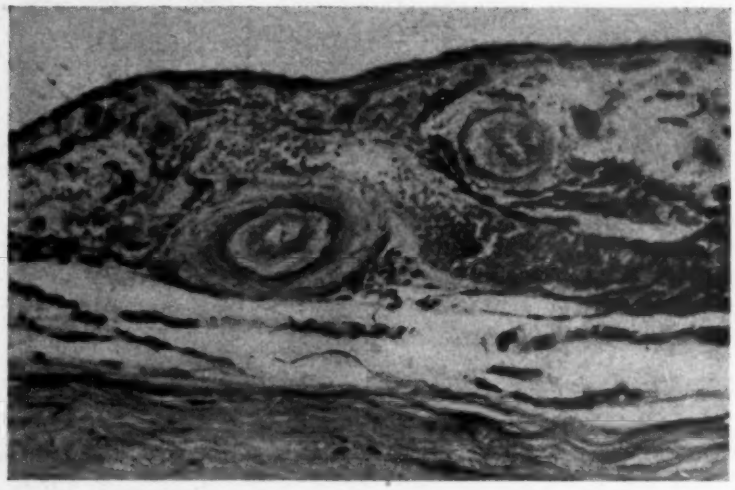

Fig. 8 (Cordes and Aiken). (Verhoeff stain, high power) Choroid. Note the marked medial hypertrophy and intimal thickening. The lumen is considerably narrowed.

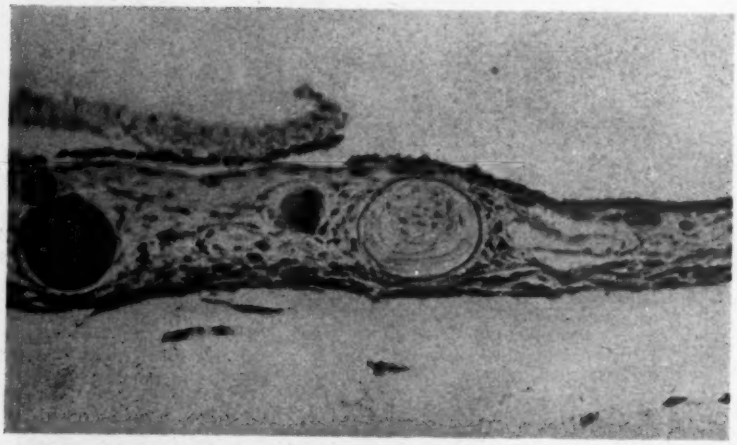

Fig. 9 (Cordes and Aiken). (Mallory connective-tissue stain, high power) Choroid. Complete occlusion of a choroidal artery due to formation of subendothelial connective tissue.

only moderate narrowing of the lumen (fig. 11). Occasional small choroidal hemorrhages were found, and there was slight diffuse round-cell infiltration. The choroidal veins, choriocapillaris and lumina were normal.

Optic nerve and disc. The disc showed marked edema, with crowding of the retinal nuclear layers away from its edge. There was patchy atrophy, with demyelinization of many nerve-fiber bundles. Surrounding, and posterior to the entrance of the central vessels into the nerve, the nerve showed marked degenerative changes, with necrosis, possibly due to occlusion of the posterior and nearby branches of the central retinal artery. This was thought to be so because the degenerated area was so sharply defined from the normal nerve tissue just a short distance

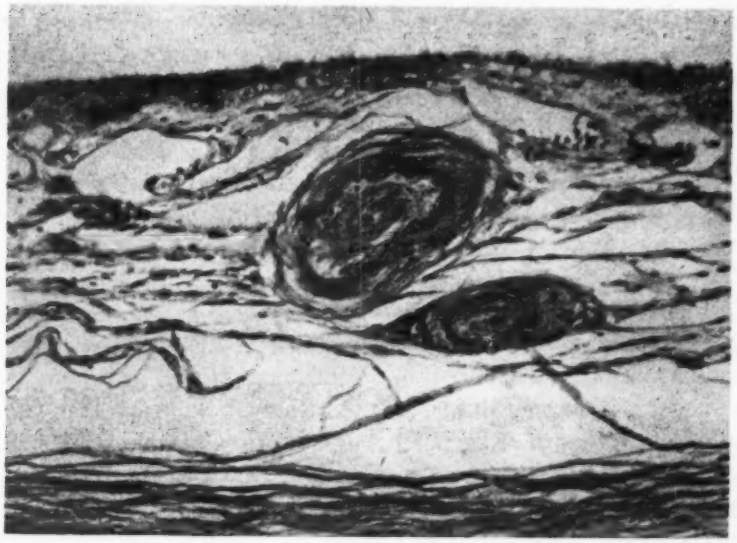

Fig. 10 (Cordes and Aiken). (Verhoeff stain, high power) Choroid. Marked intimal thickening and proliferation with obstruction of the lumen.

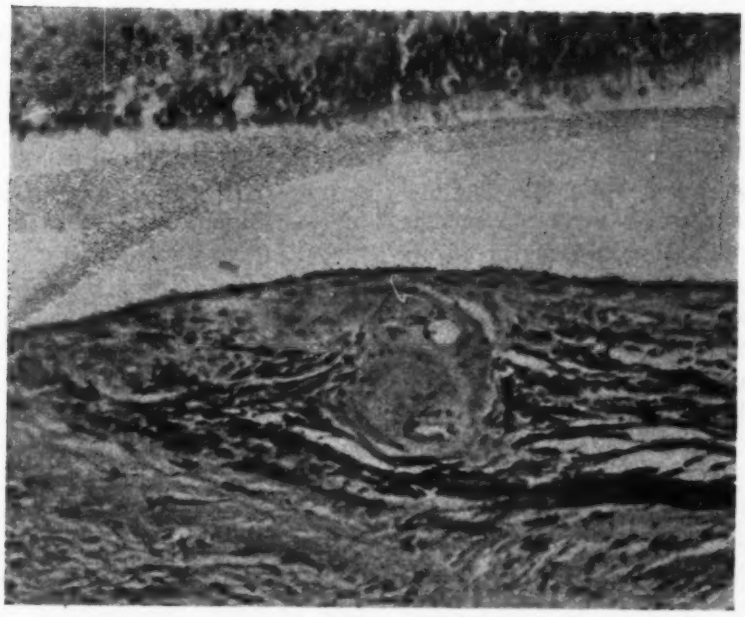

Fig. 11 (Cordes and Aiken). (High power) Choroid. There is hyalinization of the walls of the small choroidal arteries. The lumen is extremely small.

anterior to the entrance of the vessels. In this degenerated area many of the small vessels were occluded by thrombi, and had thickened walls. More anteriorly the central artery showed intimal thickening.

Comments

From an analysis of the fundus findings in the literature and from our own observations, we are not inclined to re-

gard any single fundus lesion, or combination of fundus lesions, as being pathognomonic of lupus erythematosus. It is possible, however, to arrive at several general conclusions. When the disease becomes systemic, the initial fundus changes may be limited to dilatation of the retinal vessels. At this time, or soon thereafter, cotton-wool exudates and possibly hemorrhages may appear. This so-called "toxic retinitis" is probably the most typical and frequent fundus finding encountered in lupus erythematosus. This conclusion is consistent with the opinions of Wagener[16] and others.

It is our belief that fundus changes beyond this stage are to be regarded as secondary to involvement of certain of the visceral organs, especially the kidneys and heart, and are due to widespread involvement of the arterial vascular system. This case did not come under our observation until 14 months after the onset of the disease. By that time the patient had already developed a hypertension and showed evidences of kidney damage and valvular heart disease. At this stage the retinal arterioles showed widespread organic changes in addition to cotton-wool exudates and hemorrhages, and it is not at all unlikely that these changes were nothing more than the manifestations of a diffuse hypertensive arteriosclerosis. Microscopic examination of the retina and the visceral organs tend to substantiate this conclusion. The vascular changes which were seen in this case, such as intimal thickening and sclerosis of the arteriolar and arterial walls, with narrowing and occlusion of their lumina, are characteristic of hypertension. Sections taken from the retina and visceral organs were sent to Dr. Henry P. Wagener of the Mayo Clinic, and he and Dr. J. W. Kernohan concurred in the opinion that the changes were characteristic of hypertensive-arteriolosclerosis. Dr. Kernohan was unable to find any evidence of the type of vascular lesion presumed to be characteristic of the vessels in lupus erythematosus in the retina, the kidney, or any of the other tissues. He was especially interested in the thromboses, particularly in the retinal vessels, but stated he could not diagnose them as being of lupus origin since the typical intimal endothelial changes were absent. He further believed that the retinal and renal lesions represented a diffuse arteriolosclerosis complicating the lupus, rather than an actual lupus lesion of the vessels and kidneys with secondary hypertension.

It would seem, however, that the widespread vascular occlusive lesions would fit reasonably well into the picture of lupus. These may be embolic in nature, or due to thromboses occurring at the site of a toxically damaged endothelium. The patchiness of the vascular lesions observed clinically was confirmed pathologically. Some of the retinal arterioles appeared reasonably normal while others showed hyperplastic sclerosis, narrowing of the lumina and thromboses. This thrombotic and patchy nature of the vascular lesions is not inconsistent with lupus, although this point must be left open to question.

Wagener[16] recently made the statement that "in view of the rather frequent occurrence of vegetative endocarditis in cases of acute disseminated lupus erythematosus, it is rather surprising that embolic phenomena are not observed more often in the retina." He reported such a case in which he observed an area of ischemic edema in one retina associated with closure, probably embolic, of a small terminal arteriole and, a few days before death, a number of petechial hemorrhages, with white centers, in each retina. The absence of petechial retinal hemorrhages in our patient is certainly surprising considering the fact that showers of

such hemorrhages were seen in the skin, and that at autopsy multiple emboli were observed in several of the organs, particularly the brain and lungs.

Summary

A case of acute disseminated lupus erythematosus in a 30-year-old woman was observed clinically for a period of six months before fatal termination.

Fundus examination revealed cotton-wool exudates with small irregular hemorrhages as well as flame-shaped hemorrhages. There was edema of the disc. The most striking features were the vascular changes. The veins were dilated and irregular in caliber, with perivascular thickening and small isolated venous branch thromboses. The arterioles showed a spotty and disseminated distribution of markedly irregular localized narrowings. In some areas there was complete occlusion, associated with perivascular thickening. There was also arteriolosclerosis.

Microscopic examination of the eye showed, in addition to the hemorrhage and exudates, subintimal thickening and sclerosis of the arteriolar and arterial walls with a narrowing of the lumina. There were scattered, widespread vascular occlusive lesions present. The vessels did not, however, show the intimal endothelial changes usually considered as characteristic of acute disseminated lupus erythematosus.

From a review of the literature and our own observations, we are not inclined to regard any single lesion or combination of lesions pathognomonic of lupus erythematosus. The so-called "toxic retinitis" is probably the most typical and frequent fundus picture seen in acute disseminated lupus erythematosus.

384 Post Street (8).

References

[1] Klauder, J., and De Long, P. Arch. of Ophth., 1943, v. 7, p. 856.
[2] Kierland, R. R. Proc. Staff Meet., Mayo Clin., 1940, v. 15, p. 675.
[3] Montgomery, Hamilton. Proc. Staff Meet:, Mayo Clin., 1940, v. 15, p. 678.
[4] Stickney, J. M. Proc. Staff Meet., Mayo Clin., 1940, v. 15, p. 680.
[5] Osler, William. Amer. Jour. Med. Sc., 1895, v. 110, p. 629.
[6] Rose, E., and Pillsbury, D. M. Ann. Int. Med., 1939, v. 12, p. 951.
[7] Ludy, J. B., and Corson, E. F. Arch. Dermat. & Syph., 1938, v. 37, p. 403.
[8] Stillians, A. W. Med. Clin. North America, 1942, v. 26, p. 29.
[9] Matthews, Morgan W. Tri-State Med. Jour., 1942, v. 14, p. 2670.
[10] Baehr, G., Klemperer, R., and Schifrin, A. Trans. Asso. Amer. Physicians, 1935, v. 50, p. 139.
[11] Keith, N. M. Proc. Staff Meet., Mayo Clin., 1940, v. 15, p. 682.
[12] Slocumb, C. H. Proc. Staff Meet., Mayo Clin., 1940, v. 15, p. 683.
[13] Bergmeister, R. Wien. med. Woch., 1929, v. 79, p. 1116.
[14] Pillat, A. Arch. f. Ophth., 1935, v. 133, p. 566.
[15] Keil, H. Arch. Mod. Med., 1940, v. 66, p. 339.
[16] Wagener, H. P. Amer. Jour. Med. Sc., 1946, v. 211, p. 240.
[17] Stokes, J. H., Beerman, H., and Ingraham, N. R. Amer. Jour. Med. Sc., 1944, v. 207, p. 540.
[18] Belote, G. H. Arch. Dermat. & Syph., 1939, v. 39, p. 793.
[19] Koch, F. L. P., and McGuire, W. P. Trans. Amer. Ophth. Soc., 1945, v. 43, p. 343.
[20] O'Leary, P. A. Proc. Staff Meet., Mayo Clin., 1940, v. 15, p. 686.
[21] Mallory. New England, Jour. Med., 1938, v. 218, p. 838.
[22] Fuchs, Adalbert. Die Erkrankungen des Augenh.; Vienna, Franz Deuticke, 1943, p. 143.
[23] Maumenee, A. E. Amer. Jour. Ophth., 1940, v. 23, p. 971.
[24] Klauder, J., and Ellis, V. M. Arch. of Ophth., 1939, v. 21, p. 893.
[25] Abramowicz, I., and Dulewicz, M. Ann. d'ocul., 1933, v. 170, p. 599.
[26] Kurz, O. Ztschr. f. Augenh., 1938, v. 95, p. 315.
[27] Semon, H. C., and Wolff, E. Proc. Roy. Soc. Med., 1933, v. 27, p. 153.
[28] Goldstein, I., and Wexler, D. Arch. of Ophth., 1932, v. 8, p. 852.
[29] Guion, C. M., and Adams, E. C. Amer. Jour. Med. Sc., 1943, v. 33, p. 205.

CAPILLARY FRAGILITY AND CAPILLARY PERMEABILITY IN RELATION TO RETINAL HEMORRHAGE*

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The pathogenesis of retinal hemorrhage is frequently obscure. There is at least a possibility that certain of the cases may be due to an alteration in the capillary wall which may be present throughout the body, although obvious lesions may appear only in the retina. In an attempt to explore this possibility we have carried out certain tests, especially tests intended to demonstrate increase in capillary fragility and permeability in the cutaneous capillaries, in a series of patients suffering from retinal hemorrhage. Increase in capillary fragility would be expected to cause hemorrhage primarily in vessels of capillary type. The retinal capillaries would probably share in any capillary change occurring generally.

Since the drug rutin has been shown to improve capillary fragility when tested in the cutaneous capillaries,[1, 2] and also more recently[3] to have a beneficial effect on increased capillary permeability, a clinical study of its effect on the recurrence of retinal hemorrhage was undertaken.

MATERIAL AND METHODS

Two separate groups of patients were studied. One group consisted of 47 subjects with recent retinal hemorrhage who were referred from other dispensaries of the University Hospital to a special dispensary set up for this study. This group will be subsequently referred to as the dispensary group or dispensary series. Each patient was requested to visit the dispensary at least once every six weeks. In some cases visits were more frequent and in other cases, due to faulty patient coöperation, they were farther apart. However, 37 of this group returned for from 1 to 14 follow-up studies. All patients in this group were examined ophthalmoscopically on each visit by one of us (LaM.) with careful charting so that it seems reasonably certain that all ophthalmoscopically visible hemorrhages were detected.

The second group consisted of 32 patients with retinal hemorrhage referred as private patients to one of us (J.Q.G.). This group does not include all the patients referred to (J.Q.G.) because of retinal hemorrhage, but only those referred by nine ophthalmologists who, because of association with the authors or previous experience or interest in this study, might be expected to supply accurate data and coöperation in the follow-up study. Fifteen patients in this group were followed for a period up to four years, usually every 2 or 3 months so far as the studies (by J.Q.G.) are concerned. Eyegrounds were reëxamined by the referring ophthalmologists but at more irregular intervals for this, the private group or private series, than for the dispensary group. In no case were these patients studied by the one (LaM.) who followed the eyegrounds of the dispensary group, nor in any case were the eyegrounds actually

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charted. Thus, for the private group, the occurrence of a small retinal hemorrhage, not apparent subjectively to the patient, nor noted by the ophthalmologist, nor absorbed before examination, cannot in every case be entirely excluded.

Blood pressure was measured routinely, and patients were questioned for known diabetes. Special studies included: (1) Measurement of capillary fragility based on the method of Göthlin[3] but modified so that usually only the first stage was carried out. (2) Measurement of cutaneous lymphatic flow by the dye method of McMaster.[4] (3) Measurement of plasma creatinine by the method of Steinitz and Turkand.[5] (4) Determination of cutaneous capillary mobility by capillary microscopy.[6] (5) In certain cases, bioassay for antidiuretic hormone of the pituitary gland.[7]

Studies 1 and 2 proved to be of considerable interest, and will be reported in detail. Studies 3, 4, and 5 proved to be relatively less important and will not be reported in detail, but simply considered in the discussion.

Measurement of capillary fragility

1. A circular area, 6 cm. in diameter, is marked off in each antecubital space.

2. A blood-pressure cuff is placed about each upper arm and inflated to 35 mm. Hg for 15 minutes. Thereafter, petechiae are counted, using a good light and lens.

If 2, 1, or no petechiae appear, the fragility is considered normal; if 6 or more petechiae appear, the fragility is increased; if 3, 4, or 5 petechiae appear and the test is being carried out for the first time, fragility is borderline and a second stage, as described elsewhere,[3] must be carried out; in a follow-up study, however, where the previous test was abnormal, 3, 4, or 5 petechiae are considered to indicate increased capillary fragility.

Measurements of cutaneous lymphatic flow

1. The blue colloidal dye, patent blue, is used, purified according to the method of McMaster.

2. About 0.04 cc. of the dye is injected intracutaneously, in the antecubital space, and the spread of streamers is followed for a period of 15 minutes. Spread during the first minute is due to the force of the injection, but thereafter spread depends upon the rate of lymph flow. If the spread from the 1st to the 15th minute is three fourths of an inch or more, cutaneous lymphatic flow is increased; if less than three-fourths inch, flow is normal. The color disappears, always within two days, often in 18 hours. In some 5,000 tests, no reaction has occurred nor has any permanent discoloration resulted. Rarely, a transient redness is seen about the area of injection, lasting one hour.

The significance and importance of cutaneous lymphatic flow has been considered in more detail elsewhere,[6] but it may be summarized here as follows: (a) Lymph is formed of fluid which has left the capillaries, and its rate of formation determines its speed of flow through the lymph vessels. (b) Increased rate of lymph flow can only result from increased passage of fluid through the capillary wall. (c) Increased passage of fluid through the capillary wall results when capillary pressure is increased without impediment to capillary flow, or where there is a primary increase in capillary permeability. In this sense, increased capillary pressure is thought to occur in association with fluid retention, in either renal or pituitary disease. If these conditions can be excluded, increased lymphatic flow may be presumed to be on the basis of increased capillary permeability, when it is frequently but not invariably associated with increased capillary fragility. This concept, however, as just described, has appeared

only about two years ago, so that lymphatic-flow studies are lacking in certain of the early cases of the private series.

Plan for rutin medication

The nature and use of rutin has been described elsewhere.[1, 2, 3] In general, the initial dose given was 60 mg. per day (20 mg. 3 times a day) and tests for capillary fragility and permeability, one or both depending on what findings were originally abnormal, were repeated in six weeks. The dose of rutin was increased so long as either test remained abnormal but was held constant when both tests were normal. The cases of the private series were studied every six weeks as long as either test was abnormal, and thereafter every three months, so far as possible. In general, patients in the dispensary group were seen every six weeks, regardless of the outcome of previous tests.

TABLE 1

Results in studies of capillary fragility and capillary permeability in relation to retinal hemorrhage

	Capillary Fragility			Lymphatic Flow			Both Tests	
	Increased	Normal	Total	Increased	Normal	Total	Increased	Normal
Dispensary group	23	24	47	25	22	47	12	11
Private group	24	8	32	8	15	23	7	6
Total	47	32	79	33	37	70	19	17

Results

I. Findings on initial examination

1. Capillary fragility and cutaneous lymphatic flow. (See Table 1). In the dispensary group, consisting of 47 subjects, capillary fragility was increased in 23 subjects but normal in 24; cutaneous lymphatic flow was increased in 25 subjects but normal in 22; both tests were abnormal in 12 subjects and both tests were normal in 11 subjects.

In the private group, consisting of 32 subjects, capillary fragility was increased in 24 subjects but normal in 8; cutaneous lymphatic flow was increased in 8 subjects, normal in 15, and not done in 9; both tests were abnormal in 7 subjects and normal in 6 subjects.

Considering the two series as a whole, capillary fragility was increased in 47 of 79 subjects, or approximately 60 percent. Of the 70 subjects in whom cutaneous lymphatic flow was measured, it was found to be increased in 33 persons, or 47 percent. Putting it another way, in the 70 persons in whom both tests were carried out, only 17 subjects, or 24 percent, showed normal tests for both capillary fragility and cutaneous lymphatic flow.

2. Sex incidence. In the dispensary group, there were 19 males, and 28 females; in the private group 22 males and 10 females. Thus, in the combined groups there were 41 males and 38 females.

3. Age incidence. In the dispensary group the age range was from 29 to 72 years, but 85 percent of the patients were over 40 years of age, and 74 percent were aged 50 years or over. In the private group one patient was aged 22 years, 3 were between 31 and 40 years of age, 6 more were between 41 and 50 years, and the remainder, or 22 patients, were over 50 years of age, the oldest patient being aged 82 years.

4. Incidence of diabetes. In the dispensary group, 22 of the 47 patients were

diabetic, as were 5 of the 32 in the private group, making a total incidence of 27 out of 79 patients, or 34 percent.

5. Incidence of hypertension. In the dispensary group, 19 patients were hypertensive (systolic blood pressure 150 mm. Hg or more, or diastolic 100 mm. Hg or more, or both) and 15 of the private group, making an incidence of 34 out of 79 patients, or 42 percent.

6. Incidence of diminished renal function as evidenced by elevation of plasma creatinine. In the dispensary group 7 patients showed slight elevation of plasma creatinine, as did 4 of the private group, making an incidence of 11 out of 79 patients, or 14 percent.

II. Results of rutin therapy and follow-up studies

1. Period of follow-up study. Patients in the dispensary group have been followed for 6 weeks to 13 months. Ten of the 47 patients failed to return, so only 37 are shown in Table 2. Only 15 of the private series have been followed, for a period of 6 to 51 months, averaging 13 months.

2. Effect on capillary fragility. Of the 37 patients followed in the dispensary group, 19 showed an initially increased capillary fragility. Of these, following rutin therapy with the dose and for the time interval as shown in Table 2, 9 showed fairly consistent return of test to normal, while in 10 fragility either remained consistently increased or was increased at times. It is not possible at this time to predict the result of increased rutin dosage or a longer interval of follow-up, especially as some of the patients are no longer under observation. Of the 15 patients followed in the private group, capillary fragility remained consistently increased in two and was intermittently increased in two, while in 11 it became normal.

3. Effect on cutaneous lymphatic flow. Of the 37 patients followed in the dispensary group, 22 showed an initially increased cutaneous lymphatic flow. Twelve of these showed a fairly consistent return to normal after rutin therapy, while in 10, lymphatic flow was either consistently increased or increased with sufficient frequency to make the course appear unsatisfactory. Again, one cannot predict the result of higher rutin dosage and a longer follow-up period. Of the 15 patients followed in the private group, 8 showed an initially increased cutaneous lymphatic flow. All of these have shown return to normal with one exception and that patient, a woman of 66 who has been followed for 15 months at approximately two-month intervals, had only one abnormal test in the series which preceded by three weeks her second and last retinal hemorrhage.

4. Effect on recurrence of retinal hemorrhage. In Table 2, each symbol means one study of a patient, 52 patients in all being charted. The symbol for the study made nearest the time of occurrence of a retinal hemorrhage is joined with either an h (dispensary) or H (private). In the column designated as "First Visit" all symbols are shown with either an h or H. Three patients, who had been given rutin prior to their referral to the dispensary, are listed in the "First Visit" column at their respective rutin dosages.

Six patients in the dispensary group that were followed had initially normal tests for both capillary fragility and cutaneous lymphatic flow, although three of these, at either the first or second follow-up showed one or both tests abnormal and in two instances this change occurred coincident with a fresh retinal hemorrhage. All three were then started on rutin. One patient, with initially normal studies, was seen once in follow-up, was normal at that time, and was not seen

TABLE 2

STUDY OF THE EFFECT OF RUTIN THERAPY

Rutin Dosage mg. Per Day	First Visit	After Treatment: Months 0–2	2–4	4–6	6–8	8–10	10–12	Years 1–2	2–3	3–4
None	hx = 1 ho = 3 hg = 10 HG = 11 hl = 12 HL = 1 hgl = 8 HGL = 3	gl = 1 o = 1 x = 1	hl = 1 ho = 1 l = 1		x = 1	x = 2 ho = 1	x = 2	x = 2 l = 1		
60	hgl = 1 ho = 1	hg = 2 HG = 1 o = 1 g = 4 l = 6 gl = 1 x = 6 X = 5	hg = 2 HG = 2 hl = 1 o = 1 g = 1 G = 1 l = 3 x = 6 X = 7	HG = 1 hl = 2 g = 1 L = 1 gl = 1 x = 3 X = 7	0 = 1 l = 2 x = 4 X = 7	o = 1 g = 1 x = 2 X = 4	o = 1 x = 1 x = 4	x = 1 x = 16	× = 6	X = 3
80	hx = 1	X = 1	hg = 1 O = 2	o = 2 X = 1	hl = 1 HL = 1 O = 1 X = 1	O = 1 X = 1	X = 2	X = 3	X = 3	X = 2
120		o = 1 g = 1 l = 4 gl = 1 x = 2	hg = 2 HG = 1 o = 3 g = 2 l = 1 x = 4	ho = 1 hg = 1 HG = 3 hl = 1 g = 2 l = 1 x = 4	hl = 1 o = 4 O = 2 g = 1 l = 1 x = 1	hl = 1 o = 1 O = 1 G = 1	ho = 1 HG = 1 hl = 1 o = 1 O = 2 l = 2	ho = 1 hg = 1 O = 2 g = 1 G = 1 X = 3	X = 1	
160							HO = 1 HG = 1	HG = 1		
180			hl = 1 g = 1 gl = 1	hl = 1 o = 2 g = 3 l = 1 x = 1	g = 3 l = 2 gl = 1 x = 1	o = 2 g = 2 l = 3	o = 2 g = 1	HG = 2 o = 2 g = 2 l = 1		
200				hg = 1 o = 1 g = 1	gl = 2	ho = 1 hg = 1 o = 1 l = 1	o = 1 g = 2	hg = 1		
240				l = 1	hg = 1 o = 3 g = 1	g = 2 gl = 1 x = 1	g = 1 gl = 1	HG = 1 o = 1		
280						hg = 1	l = 1	HG = 1 o = 1 g = 1		
400 and +							hg = 1	hg = 1 HG = 1 g = 1 G = 1 gl = 1		

since. The remaining two patients (of the six) were taking rutin at the time they were first seen in the dispensary. This was continued for a time. On subsequent follow-up one patient showed a fresh retinal hemorrhage, and both tests were abnormal. His dose of rutin was increased. The last patient was normal on follow-up, his rutin was discontinued, and he has remained well since and his tests have remained normal.

Thus, all but one of the patients charted in Table 2 took rutin at least at some time. Those indicated as not taking rutin after the sixth month represent cases that lapsed treatment, at least temporarily.

In the dispensary group, 18 of the 37 patients had at least one retinal hemorrhage during the follow-up period, and in five cases the hemorrhage was sufficient to affect vision and be subjectively noted, while in the remainder it was recognized only by ophthalmoscopic examination. In the private group, three of the patients had recurrent hemorrhage, all sufficient to affect vision.

Since several patients had more than one hemorrhage, it is apparent from Table 2 that a total of 51 retinal hemorrhages occurred in 21 persons during the period of observation. In these, there was an associated increased capillary fragility 32 times, increased cutaneous lymphatic flow 12 times and, on seven occasions, hemorrhage occurred when both tests were normal. As Table 2 shows, hemorrhage occurred three times in persons not taking rutin, at least at the time preceding the hemorrhage.

5. Rutin dosage. As shown in Table 2, dosage ranged from 60 mg. per day to about 400 mg. per day, but 90 percent of the subjects studied were given 180 mg. per day or less. Three subjects who were followed longer than 2½ years were started on hesperidin (which does not appear in the table) but changed over to rutin about that time. Hesperidin has a chemical formula much like rutin, and was used by us originally. As a rule, the crude preparation of hesperidin acted like rutin, but the refined preparation was much less active and the crude preparation varied in potency. When rutin, a chemically pure substance which was uniformly active, became available, it was substituted in all cases for hesperidin.

Discussion of results

The incidence of elevated plasma creatinine, hypertension, diminished capillary mobility (9 cases), and positive bioas-

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Explanation: Each symbol appearing alone or in combination with another symbol, represents one period of study.

g,G indicates increased capillary fragility.

l,L indicates increased capillary permeability (increased cutaneous lymphatic flow).

x,X indicates a period of study in a patient whose general course is favorable in that retinal hemorrhage has not recurred and that capillary fragility and permeability are normal with fair consistency.

o,O indicates a period of study in a patient whose general course is unfavorable in that, while tests for capillary fragility and permeability are normal at the time of that study, they are either not normal consistently or, some time during the course of the study, a retinal hemorrhage has occurred.

h,H in combination with any other symbol means that a retinal hemorrhage has occurred near the time of the study.

g,l,x,o,h indicate patients of the dispensary group.

G,L,X,O,H indicate patients of the private group.

It should be noted that a patient represented by x or X is always represented by the same symbol, whereas unsatisfactory cases may be represented, depending on the findings, by g,l,o,h or G,L,O,H. By definition of a satisfactory case, h or H cannot appear combined with x or X, after treatment has been begun. The number associated with a symbol or symbol group indicates the total similar tests for that period, but this cannot always be translated into total number of patients since, especially for the longer periods, the same patient may appear more than once.

say for antidiuretic hormone (8 cases) did not significantly influence the results of therapy, and have not been reported in detail. Some difference might appear, however, in a larger series, and it is a clinical impression that the occurrence of any of these factors makes chance for success with therapy a little less likely. The same can be said for diabetes, although here the evidence is suggestive, but not absolutely significant.

It is quite apparent, however, that there is no relation between the degree of elevation of systolic and diastolic blood pressure, in subjects with hypertension, and the incidence of retinal hemorrhage.

The relation of increased capillary fragility and increased cutaneous lymphatic flow with retinal hemorrhage is significant, both in the initial hemorrhage and in recurrence, although it is obvious that a direct relationship seems to exist for only a certain group of the cases. There are undoubtedly cases where retinal hemorrhage occurs entirely apart from any change in general capillary fragility and permeability.

However, the role of rutin in correcting this capillary condition and, perhaps, thereby avoiding further hemorrhage is less clear. Rutin has been less effective in correcting increased capillary fragility and permeability in the present series than in the series of hypertensives previously reported,[3] and the dosage required has frequently been larger. Moreover, certain patients have had recurrence of retinal hemorrhage even while tests for capillary fragility and permeability have been normal, so that one must conclude that additional factors are present in these cases or, perhaps, the initial hemorrhage has somehow predisposed to recurrence. Also, it should be noted that results appear to be better in the private than in the dispensary group, which may be due to difference in economic status, or difference in sex predominance (more males in the private group, more females in the dispensary group), or simply a difference in completeness of ophthalmoscopic charting in which case the difference would be apparent rather than real. Unfortunately, it has not been practicable to study an untreated group, but it seems probable, but not absolutely certain, that rutin in some cases has been useful in preventing further retinal hemorrhages.

Summary and Conclusions

1. A considerable number of patients with retinal hemorrhage have an associated generalized capillary abnormality, as shown by abnormal response to tests for capillary fragility and permeability carried out on the vessels of the skin. The present series showed about 75 percent of such incidence for either one or both tests, and this is considered significant since these tests are uniformly negative in perfectly normal individuals.

2. Recurrent retinal hemorrhage, occurring during the period of study, was usually but not invariably associated with either increased capillary fragility or permeability, as shown by the tests.

3. In the series studied, rutin therapy was followed by return of tests to normal in about half of the dispensary group and in about 70 percent of the private group and such subjects usually, but not invariably, failed to develop further retinal hemorrhage. Considering the number of cases, the period of follow-up, and the scatter of results, final conclusions cannot be drawn, but it is at least suggestive that rutin, in adequate dosage and given over a long enough period, may be of value in preventing further retinal hemorrhage in that group of patients where the initial hemorrhage was associated with a generalized capillary fault.

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References

[1] Griffith, J. Q., Jr., Couch, J. F., and Lindauer, M. A. Effect of rutin on increased capillary fragility in man. Proc. Soc. Exp. Biol. & Med., 1944, v. 55, p. 228.

[2] Shanno, R. L. Rutin: New drug for treatment of increased capillary fragility. Amer. Jour. Med. Sci., 1946, v. 211, p. 539.

[3] Griffith, J. Q., Jr., and Lindauer, M. A. Rutin: Therapy for capillary abnormality in hypertension. Ohio State Med. Jour. In press.

[4] McMaster, P. D. Changes in cutaneous lymphatics of human beings and in lymph flow under normal and pathologic conditions. Jour. Exper. Med., 1937, v. 65, p. 347.

[5] Steinitz, K., and Turkand, H. The determination of glomerular filtration by the endogenous creatinine clearance. Jour. Clin. Invest., 1940, v. 19, p. 285.

[6] Griffith, J. Q., Jr., and Lindauer, M. A. The medical treatment of hypertension. Clinics, Philadelphia, J. B. Lippincott Company, 1946, v. 5, p. 82.

[7] Griffith, J. Q., Jr., Corbit, H. O., Rutherford, R. B., and Lindauer, M. A. Studies of criteria for classification of arterial hypertension: V. Types of hypertension associated with the presence of posterior pituitary substance. Amer. Heart Jour., 1941, v. 21, p. 77.

THE EFFECT OF VISUAL TRAINING ON EXISTING MYOPIA*

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This research was undertaken in an effort to determine the value of visual training as a means of improving the visual acuity in patients with myopia. During the past few years, ophthalmologists have often been questioned by the parents of myopic children and by myopic individuals relative to the possibility of improving their sight, or of overcoming their near-sightedness, so that they might no longer have to wear glasses to see well at a distance. These queries have become so frequent that it seemed incumbent upon ophthalmologists to try to evaluate such methods of training as are employed by many optometrists and a few ophthalmologists.

The first efforts to improve vision by means other than glasses that received wide public attention were those advocated by the late W. H. Bates, M.D., who caught the public notice by means of a book entitled *Perfect Sight Without Glasses*, published in 1920. This idea, so fascinating to the wearers of glasses and especially to those who were forced to use strong corrections, naturally had great appeal and his training program developed a considerable following. The fact that very few have been able to dispense with their glasses is sufficient evidence of the ineffectiveness of the method. The idea, however, was so attractive that it was seized upon and efforts made to find more satisfactory methods than the Bates training for accomplishing the same purpose.

Many different training techniques have been studied and are employed. Most of them, however, have a common background of thought that has been standardized to a considerable degree in some of

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the optometric schools of the United States. Variations in details are, of course, practiced by almost everyone who gives this type of training. For the purpose of this study a method that closely approaches the most frequently employed ideas was used and will be given in detail later in this article. Longer or shorter periods of training might have produced different results. Two of the most outstanding cases of improvement observed during this time were not treated in this group, but by a practitioner not engaged in this particular project.

Although visual training for myopia had been in use for a number of years by optometrists at the time of the inception of this program, there was no report found in the American ophthalmic literature of a series of cases of myopia in which such training had been done with careful ophthalmologic examinations. It is interesting that coincidental with our study a somewhat similar one was being carried out in Baltimore. A series of 103 patients has been reported by Alan Woods, M.D., in the *American Journal of Ophthalmology* for January, 1946. Their work differed in that the entire training program was controlled by an independent group of optometrists whose detailed technique was not reported, although ophthalmologists of the Wilmer Institute examined the cases before and after training.

Experimental procedure

There are obviously innumerable phases to the problem of exercises in myopia, so it seemed best to attempt only a small part of the study in order that one phase at least could be comprehensively investigated; hence, the limitation to the study of the possibility of improving vision of myopic patients by training. Other pertinent questions are: How long does improvement, if any, continue? In what types of myopia is the training most effective? Does the treatment have any effect on the rate of increase in progressive myopia? What would be the effect on other refractive states, as hyperopia, astigmatism, an anisometropia? What is the mechanism by which improvement, if any, is brought about?

As the primary objective of the problem as outlined was the determination of the possibility of improvement of the visual acuity in the myopic patient, it was evident that the group of patients should be standardized as much as possible, eliminating variables and unfavorable conditions so as to obtain the maximum improvement in the myopic factor. Because of this, the following standards were decided on: (1) Age 10 to 30 years. (2) Range of myopia in the greatest meridian: −0.50D. sph. to −3.00D. sph. (3) Astigmatism of 1 diopter or less. (4) No anisometropia of more than 1 diopter. (5) Correctible visual acuity of at least 20/20 in each eye. (6) No abnormal heterophoria, fusional defects, or substandard accommodation. (7) No internal or external organic condition.

The actual investigation resolved itself into the following steps: (1) The preliminary ophthalmologic examination. (2) The optometric survey. (3) The actual visual training. (4) The final ophthalmologic survey. (5) The analysis of the results. (6) The interpretation of the results with any possible conclusions.

In order to study the subject as intelligently as possible, it seemed wise to utilize the services of optometrists who were giving this type of training and of ophthalmologists who had not used these methods. Accordingly a team was formed for this study composed of ophthalmologists, optometrists, and opticians. The following arrangement of the team was decided upon: For the actual training, J. R. Bockhorst, O.D.; for the preliminary and final ophthalmologic surveys, H. Rommel Hildreth, M.D., William H. Meinberg,

M.D., Benjamin Milder, M.D., and T. E. Sanders, M.D.; and as a consulting group, E. C. Ebeling, O.D., Lawrence T. Post, M.D., and J. L. Stevenson. A full-time technician, Mrs. Harriet Thursby, did the majority of the actual training under the direct supervision of an optometrist.

Ophthalmologic examination

The ophthalmologic examination was divided among several individuals, the conditions and the examiner remaining constant for all patients examined. On the first visit (T. E. S.) a short history was taken including familial tendencies toward myopia, the length of time that myopic correction had been worn, the date of the last change, and the frequency of change of correction as related to progression. A general external and ophthalmoscopic examination was then made. Finally, the uncorrected visual acuity at 20 feet was determined with a Snellen letter chart. If the vision was less than 20/100, a shorter distance with the 20/100 letters was used. It was thought that this line would be more accurate than the 20/200 letter when used as a "walk-up," as it interpolates between 20/100 and 20/200.

Obviously the accurate determination of the visual acuity is the essential of the whole program. Theoretically a chart that is variable with similar and unfamiliar characters, as the Landolt broken ring, is much more desirable as it eliminates memory and past experience. At the beginning of the series the Landolt ring was used along with the ordinary Snellen chart with constant illumination. Three different Snellen charts were used interchangeably to eliminate memory. It was found early that lack of correlation between the Landolt and the Snellen charts was so great that it was difficult to interpret the results satisfactorily. The results with the Snellen chart alone were consistent and satisfactory. These findings were also consistent with those of the optometrist using a Projecto-Chart. On the first visit the optometric examination (J. R. B.) was also done, as it was considered necessary to do this before a cycloplegic was used. This procedure is given in detail later.

On the next visit (H. R. H.) homatropine (2 percent) was instilled at 10-minute intervals for five times. Following this, a retinoscopy and a static refraction were done. The residual accommodation was then measured. At the third visit (B. M. and W. R. M.) a postcycloplegic refraction was done and the ocular muscle balance examined, which included: (1) The near point of accommodation as measured with Prince's rule; (2) the near point of convergence; (3) the degree of fusion as found on the synoptophore; (4) the lateral and vertical muscle balance at 20 feet and 16 inches as determined with prism dissociation; and (5) the lateral and vertical fusional amplitudes as determined with rotary prisms.

Following this preliminary examination, the patient was then referred for visual training (J. R. B.) as outlined hereafter.

After completion of the visual training the above ophthalmologic examinations were repeated exactly. At this time the individual patients were qustioned as to their ideas of the value of the training and their opinion as to any subjective improvement in vision.

Optometric examination routine

The optometrist giving the training submitted a very detailed report on the examination routine and training technique he used throughout the program. This is available in the files of the Oscar Johnson Institute for those desiring to refer to it. A brief outline of this routine is as follows:

Steps 1 and 2. Visual acuity at 20 feet without correction and with habitually worn glasses.

Steps 3 and 4. Near vision with and without glasses.

Step 5. Measurement of interpupillary distance.

Step 6. Ophthalmoscopic examination.

Step 7. Ophthalmometric measurements.

Steps 8 and 9. Phoria test at 20 feet and 16 inches with habitually worn glasses. A 6-degree prism was placed base up and the horizontal phoria measured by the Risley rotary prism.

Step 10. Static retinoscopy at 20 feet.

Step 11. Dynamic retinoscopy at 20 inches.

Step 12. Dynamic retinoscopy at 40 inches.

Step 13. Subjective refraction test at 20 feet.

Step 14. Horizontal phoria at 20 feet with correction found in Step 13.

Steps 15 and 16. Adduction and convergence at 20 feet.

Step 17. Abduction at 20 feet.

Step 18. Vertical phoria test at 20 feet.

Step 19. Horizontal phoria at 16 inches with correction found in Step 13.

Steps 20, 21, 22, and 23. Listed as monocular and binocular cross-cylinder tests at 16 inches. A cross-cylinder was placed before each eye and a gridlike target observed. Spherical lenses were changed until the vertical and horizontal lines on the grid appeared alike.

Steps 24 and 25. Positive and negative fusional reserve relative convergence at 16 inches.

Step 26. Vertical phoria at 16 inches.

Step 27. Amplitude of accommodation.

Steps 28 and 29. Positive and negative relative accommodative reserve.

The detailed report ends with the sentence, "The 29th step completes the tests used and provides the basis for diagnosis of the subject's functional visual problem."

Technique of visual training

The procedure outlined here required the use of an Arneson Squint Corrector, a Keystone Tel-Eye Trainer with certain Keystone cards whose numbers are given later, and an American Optical Company Wells-Head. The technique was broken into 11 individual steps laid out for a training period of 24 days averaging about one hour per day.

First Sequence, Six Days of Training

Step 1. Subject was seated before the Arneson Squint Corrector approximately 20 inches from the instrument. The instrument was equipped with a large disc with a medium-sized fixation target that could be rotated clockwise and counterclockwise. The right eye was occluded with a patch. The instrument was started rotating clockwise with instructions to the subject to fixate constantly the medium-sized target as it moved in a circular fashion. While fixating the target, his attention was also directed to the referential background of the disc which consisted of a black, red, and blue "E." The disc was rotated for three minutes. After the three-minute period the instrument was reversed to a counterclockwise direction, the whole procedure being repeated for three minutes. The same procedure was repeated occluding the left eye. Total working time for each eye was six minutes.

Step 2. Subject was placed before the Tel-Eye Trainer. The instrument was set at infinity position on the graduated slide, using Rotor 4 giving a four-second flash. No lenses were used. Two sets of cards were used, different sets on alternate days. The sight of the right eye was blanked out by manual push-button control and the left eye only was permitted to view the card, BO1-EC1. There were numbers interspersed throughout the field of the picture and the subject was instructed to locate the numbers in sequence from 1 to 10. If the picture or numbers appeared blurred, no changes or alterations were made in the setting of the instrument. The subject was instructed to keep watching the card until the numbers began to clear. This training was continued for five minutes. For training of the right eye the instrument setting remained the same with the exception that the left eye was now blanked out and Card BO1-EC3 inserted. This card was the same as the first with the exception that the numbers were in different positions throughout the field. On alternate

days Cards AN18 and AN16 were used in the same manner. Instructions in procedure remained the same. Step 2 was all monocular training.

Step 3. Subject remained at the Tel-Eye Trainer. No lenses were used. Slide remained at infinity and Rotor 4 was used. Both eyes were uncovered and for five minutes the Card BU5 was used with the subject seeing a picture of a room with the right eye in black and white, the left eye viewing a solid red field with numbers scattered through the field from 1 to 7. Instructions were to fuse the two unlike backgrounds into a single picture with the subject locating the black numbers and attempting to maintain clearness. When blur was reported, the setting of the instrument remained the same with emphasis placed on the subject's concentration to clear the numbers in spite of blur. Card BU5 was removed and Card BU6 inserted. The subject now viewed the black and white background picture in front of the left eye with a solid red field in front of the right eye, with numbers interspersed in the background from 1 to 8. The same instructions were given to the subject in viewing this card as in Card BU5. The procedure covered five minutes. Step 3 was monocular training in binocularity. Total training time for Step 3 was 10 minutes.

Step 4. Subject remained at the Tel-Eye Trainer. The instrument was set to flash alternately using Rotor 3 (3-second flash). Cards BO1-EC2 and BO1-EC4 were used. These cards were the same as the cards noted in the second step with the exception that the numbers were scattered in new positions. Instructions to the subject were to clear the numbers and the picture alternately with each eye. The second series of cards used in Step 4 were the AN1 and AN3. The cards of series one and two were used on alternate days. The AN1 card was a yellow background card with numbers arranged in a circle and a star figure in the center connecting the numbers. When the alternating flash was started, the subject located the number 1 with the right eye, the number 2 with the left eye, number 3 with the right eye, number 4 with the left eye, and so forth, until he had gone through 12 numbers. Procedure was repeated for five minutes. The AN3 card was a similar card with these exceptions; the background of the card was now white with considerably smaller numbers. In addition to locating the numbers alternately, the patient was instructed to see the numbers clearly. Step 4 was an alternating monocular training procedure.

The above four steps were repeated for six days. Beginning the seventh day Step 5 was started, all of the previous steps being discontinued.

Second Sequence, Six Days of Training

Step 5. Subject was placed before the Arneson Squint Corrector, disc approximately 20 inches from the subject. A vertical dissociating prism, 6 degrees base up, was placed before the right eye. A vertical displacing prism, 4 degrees base down, was placed before the left eye. The subject was instructed to see two targets constantly. The instrument was turned on, rotating clockwise, with instructions to concentrate attention on the top target for 10 to 15 turns, always being aware of the lower target. Attention was then directed to the lower target as the fixating target for 10 to 15 turns with instructions to the subject always to be aware of the upper target. The procedure was followed for five minutes. The change in the prism setting was as follows: a 4-degree prism, base down, was now placed before the right eyes and a 6-degree prism, base up, was placed before the left eye with the same instructions followed for five minutes in the viewing of the two targets.

Step 5 was a rotation exercise, monocularly, in binocularity.

Step 6. Subject was placed before the Tel-Eye Trainer. The instrument was set at infinity on the slide, using Rotor 2 (2-second flash). Both eyes were uncovered. Cards BU8 and BU7 were used in the slide holder. When viewing Card BU8, the subject had a black and white picture in front of the left eye and a red and blue background in front of the right eye with numbers scattered throughout the red and blue field from 1 to 8. The color arrangement of the picture in front of the right eye was that the top half was red, the lower half blue. When the light flashed on, the black and white picture and the red and blue backgrounds had to be fused into one. The numbers scattered in the red and blue fields had to be clear. Procedure was followed for five minutes. Then Card BU7 was inserted into the instrument, which card was exactly reversed as compared to Card BU8. The black and white picture appeared in front of the right eye, the red and blue background appeared in front of the left eye. Numbers ranged from 1 to 9 in the colored field. The same instructions to clear numbers were given for this card. Procedure was followed for five minutes. Step 6 was monocular training in binocularity.

Step 7. Subject remained before the Tel-Eye Trainer instrument. Slide remained set at infinity, using Rotor 8 which gave alternate flash followed by binocular flash. Cards placed in the instrument card holder were ST2, Series I. This series consisted of three cards that produced stereoscopic vision and had control marks located in this sequence: Control marks on Card 1 were set toward the left side; control marks on Card 2 were located centrally; and control marks on Card 3 were located to the right. The subject was instructed to see the pictures clearly and to fuse the control marks into a perfect cross. Each card was left before the subject for a period of five minutes. On alternate days ST2, Series II, were used with the same instructions to the patient as covered in the Series I. Step 7 was training in stereoscopic development and binocular control.

Step 8. Subject remained seated before the Tel-Eye Trainer. Slide holder was moved into the 2.50 position. Light flash, using Rotor 7, was set to operate simultaneously before both eyes. Cards SST2 were placed in the card holder. The series used were the cards numbered 0115, 0118, and 0113. Each card was viewed for five minutes. Subject's instructions were to fuse the cards into a single clear picture with emphasis being placed on his ability to produce a perfect cross of the control marks which appeared first to the left, next to the center, and lastly to the right. Step 8 was training in near-point stereopsis and binocular control.

Third Sequence, 12 Days of Training

Step 9. After Steps 5, 6, 7, and 8 had been repeated for six days, a reëxamination was made after which the third phase of the visual training was instituted. Step 9 was the repetition of Step 7.

Step 10. Repetition of Step 8.

Step 11. Part I. Subject was placed before the Wells-Head. Steady light was used. Cards were placed at four inches and an auxiliary pair of plus-10 lenses was put in the instrument. Rotary prisms were placed before the subject's eyes. This setting produced a stereoscopic effect. At the zero markings, the subject looked at Card E2 with instructions to see the object with clearness and a sense of depth. The subject received frequent rest periods by closing eyes for approximately five seconds at a time. The rotary prisms were turned base out two degrees at a time with the caution to the subject that

the card must remain clear and single. The strength of the rotary prisms was constantly increased in these 2-degree, base-out jumps until the subject could maintain single and clear vision through a total of 32 degrees, base out, 16 degrees over each eye. Training on this card was performed for five minutes. For five minutes Card C4 was placed before the patient. Rotary prisms were started at 0, again increased two degrees base out at a time until a total of 32 degrees prism base out was reached, 16 degrees over each eye, with the same instructions that the object must appear clear and single. Card 6CM was then inserted. Rotaries were placed at 0 and increased in 2-degree steps until a total of 32 degrees prism base out, 16 degrees over each eye, had been reached with the same instructions to the patient that the target must be clear and single. Total training time was 15 minutes.

Step 11. Part II. Subject was placed before the Wells-Head. A 6-degree prism, base in, was placed in the instrument. The target viewed first was a type approximately Jaeger 3. The target was set at the 16-inch mark on the reading rod. The instructions to the subject were that the print must remain clear and single at all times. Then plus lenses were introduced in ¼-diopter steps with the instruction to the subject, as the lens was changed, that again the print must remain clear and single. At the first increase of plus in the ¼-diopter steps that produced a very slight blur, the subject was told to attempt to sharpen the print. When it became impossible for the subject to improve vision with increase in plus, the 6-degree prism, base in, in the rotaries was reduced two degrees at a time until the prisms were back to 0. At this time alternate size types of print were used varying between the original Jaeger 3 down to Jaeger 1.

The above steps, 9, 10, and 11, were continued for 12 visits. Again the subject was examined. Only those patients that appeared to have the ability to accomplish any further results in the above handling were permitted to repeat for an additional 12 visits.

Steps 9, 10, and Part I of 11 were used in those cases that appeared to be a basic problem of faulty convergence ability.

Steps 9, 10, and Part II of 11 were used in those cases that appeared to be a basic problem of faulty accommodative faculty.

Results

This study represents a series of 87 patients examined, but a number of others were refused because of obvious defects. Thirty-three cases were either rejected or incomplete so that 54 case records were available for study. The majority of these patients were obtained by referral from the private practices of a number of St. Louis ophthalmologists, but some were referred by interested local optometrists. The series was not larger because of the strict limitations listed above.

As expected, no change was noted in the external or ophthalmoscopic examination of any patient. In no case was there any significant difference in the cycloplegic refractions done before and after the period of visual training. There was no more than one diopter of residual accommodation under cycloplegia remaining in any instance.

There was no appreciable effect of the visual training on the near point of convergence, near point of accommodation, or the fusional ability. About 50 percent of the cases showed an increase in esophoria of at least five prism diopters, or a decrease in the exophoria of about the same amount. In almost one half of the cases there was an increase of at least 10 prism diopters in adduction (positive fusional amplitude). There was no apparent

TABLE 1

PRE- AND POSTTRAINING VISUAL ACUITY, THE PATIENTS BEING REPRESENTED BY THEIR SPHERICAL EQUIVALENT

	5/100	10/100	12/100	15/100	20/100	20/70	20/50	20/40	20/30	20/25	20/20	Total
5/100		−2.50										1
10/100		−3.00 −2.75 (3)		−2.50 −3.00								6
12/100					−2.25		−2.50					2
15/100				−2.50 −2.75	−1.75	−2.25						4
20/100					−3.00 −2.75 −2.50 −2.00 −1.75 (2)	−3.00	−2.50					8
20/70						−3.00 −2.25 (2) −2.00 −1.75 (2) −1.50 (3)	−2.25	−2.00 −1.50 −1.25 −1.00				14
20/50							−2.25 −2.00 −1.50 −1.25	−0.75	−1.25			6
20/40								−1.25 (3) −1.00 −0.75	−1.50 −1.25 (2) −0.50	−1.00 −0.75		11
20/30											−0.75 −0.50	2
20/20												0
Total	0	5	0	4	8	11	7	10	5	2	2	54

TABLE 2

DISTRIBUTION OF ALL CASES

	Group 1 Myopia −1.00 sph. and under	Group 2 Myopia −1.25 sph. to −2.00 sph.	Group 3 Myopia −2.25 sph. to −3.00 sph.	Total
No Change	2 cases 22% of Group 1	15 cases 65.2% of Group 2	13 cases 54% of Group 3	30 cases 55% of all cases
Questionable Change	2 cases 22% of Group 1	4 cases 17.4% of Group 2	6 cases 27.2% of Group 3	12 cases 22.2% of all cases
Improvement	5 cases 55% of Group 1 Average Change—12.1%	4 cases 17.4% of Group 2 Average Change—18.7%	3 cases 13.6% of Group 3 Average Change—35.7%	12 cases 22.2% of all cases Average Change—27.1%
Total	9 cases 16.6% of all cases	23 cases 42.6% of all cases	22 cases 40.7% of all cases	54 cases 100%

relationship between the amount of the myopia and the effect of the visual training on the muscle balance. There seemed to be no relationship between the induced changes in the muscle balance and the final visual result.

As our patients had no, or only small amounts of, astigmatism and of anisometropia, the refractive error of the fellow eyes of all of our patients were quite similar. Because of this, the average spherical equivalent of each patient based on his homatropine refraction could easily be determined. On this basis we were able to divide our patients into three groups: Group 1, those patients with average myopic errors of one diopter or less; Group 2, those patients with average myopia from −1.25 sphere to −2.00 sphere; and Group 3, those with average errors from −2.25 sphere to −3.00 sphere. It was also noticed that rather than try to analyze changes in the vision of separate "eyes," it was much more satisfactory to tabulate the binocular vision, particularly as this is the actual useful vision of the patient. Table 1 shows the pre- and post-training acuities of all the 54 patients, each patient being represented by his spherical equivalent.

The problem of how to evaluate an actual change in visual acuity on an accurate quantitative basis is extremely difficult. The simplest method is merely the number of lines improvement as measured on the ordinary Snellen chart. This presupposes that the difference between each line is the same, which is obviously untrue. Another method, which Woods used in evaluating his results, determines any improvement in terms of percentage points. This is done by determining the difference in the percentages of visual efficiency of the pre- and posttraining visions, using the tables developed in industrial ophthalmology for evaluation of losses in visual efficiency following in-

jury. As Woods points out, this weighs the results in favor of the higher degrees of myopia, in as much as a case with improvement from 20/200 to 20/100, or one line, shows an increase of 28 percentage points in contrast to a case with improvement from 20/50 to 20/20, four lines, which totals 22 percentage points. Obviously, this is not valid either clinically or statistically.

After studying our cases, it was evident that the easiest method was a simple qualitative one. Thirty patients, or 55.5 percent, showed no change in the visual acuity following the course of visual training. No patient had a reduction in vision. Twelve patients, or 22.2 percent, showed a questionable improvement which consisted of a change of one line or less in acuity. It was thought that this improvement was meaningless as it was within the limits of error. This is especially true since the patients during the period of training did not wear their ordinary corrections, thus giving them experience in the judgment of blurred images. Twelve, or 22.2 per cent, of the patients showed definite improvement of vision. These results in relation to the three separate groups are shown in Table 2. Using the visual efficiency table given in Snell's *A Treatise on Medicolegal Ophthalmology,* the improvement in percentage of visual acuity was found to average 27 percent in the favorable cases.

Group 3, those with an average myopia of −2.25 sphere to −3.00 sphere, consisted of 22 patients. Of these only three, or 13.6 percent, showed any appreciable improvement. There were six with some change and 13 with no change. The three cases representing improvement changed from 15/100 to 20/70, 20/100 to 20/50, and 12/100 to 20/50. This represents an average improvement of 35.7 percentage points.

Group 2, consisting of patients with average myopia from −1.25 sphere to −2.00 sphere, included 23 cases. No change was noted in 15 cases and questionable changes in four. Four, or 17.4 percent, showed real improvement averaging 18.7 percentage points. These included three with change from 20/70 to 20/40, and one with improvement from 20/50 to 20/30.

Group 1 consists of nine patients with a myopic error of one diopter or less. Two each showed no change and questionable improvement. Five, or 55 percent, of these patients with small errors showed definite improvement with an average improvement of only 12.1 percentage points. Two of these patients showed improvement from 20/30 to 20/20, these being the only ones with improvement to 20/20. Two showed change from 20/40 to 20/25 and one 20/70 to 20/40.

A late recheck of the visual acuity was possible in 11 of the 12 cases showing improvement, the interval between the posttraining acuity and the final acuity ranging from 15 months to 23 months. These results are found in Table 3. It will be noted that five (Nos. 2, 3, 4, 5, and 10) retained all of their improvement, while three (Nos. 1, 6, and 7 reverted to their pretraining acuity. Two (Nos. 8 and 11) retained a slight improvement, while only one (No. 9) lost vision over the pretraining acuity.

Conclusions

In the first place, we realized before undertaking this problem that, no matter what our results, they would probably be criticized by both proponents and opponents of this controversial subject. If our percentage of improvement was not high enough to please the proponents, it would be charged that our technique of training was inadequate, omitting a critical or essential step. On the other hand, those who doubt that visual acuity can be altered by

such training will say that the methods of taking the vision were at fault and that removing a person's glasses will improve his unaided vision within a period of weeks without training.

Although different techniques or a larger and more varied series of cases might alter our exact figures, we believe that study of these results shows that vision in certain myopic individuals can be improved by training. Even if we group in each series is 27 percent.

As might be expected, the best results occurred in the cases of low myopia of one diopter and under (55 percent improvement). There is less defect to be overcome in these cases and the better initial vision would probably make training easier. Although the series is not large enough to give accurate figures, the results of Group 2 (17.4 percent improvement) and of Group 3 (13.6 percent

TABLE 3

LATE VISUAL ACUITIES

Group	Patient	Spherical Equivalent	Pre-training Acuity	Post-training Acuity	Interval Months	Final Acuity	Result
Group 1	1	−0.75	20/30+3	20/20−4	15	20/25−2	Unchanged
	2	−0.50	20/30	20/20	16	20/20−3	Retained Improvement
	3	−0.75	20/40−2	20/25−3	16	20/25−3	Retained Improvement
	4	−1.00	20/40+1	20/25−1	19	20/20−3	Retained Improvement
	5	−1.00	20/70	20/40−3	15	20/40+3	Retained Improvement
Group 2	6	−1.25	20/50+2	20/30+3	16	20/40−2	Unchanged
	7	−1.50	20/70+1	20/40+1	17	20/70+	Unchanged
	8	−2.00	20/70	20/40+3	16	20/50+3	Partially Improved
Group 3	9	−2.25	15/100	20/70−1	23	10/100	Worse
	10	−2.50	12/100	20/50−1	22	20/50+2	Retained Improvement
	11	−2.50	20/100	20/50−3	18	20/70+1	Partially Improved

ignore the figures of the whole group showing improvement in 22.2 percent of our patients averaging 27.1 percentage points, this contention can be proved by the results in individual patients.

It is surprising how closely these figures compare with those of Woods. His favorable group, consisting of those patients showing a consistent improvement of each eye of at least 10 points, makes up 29 percent of his entire series compared to our figure of 22.2 percent showing definite improvement. It is interesting that the average improvement of the favorable improvement) are quite similar. As Woods was unable to divide his cases on a basis of amount of myopia, these results cannot be compared.

On first study there seemed to be little direct evidence from our results as to the exact mechanism of the visual improvement. It is apparent that there is no change in the amount of the refractive error. There is also no indication of significant change in the ocular neuromuscular mechanism, such as might give rise by relaxation of the lens to a "negative accommodation." The impression gained

from these patients was that much of the improvement occurred at the cerebral level rather than in the retina. Although there was no method for absolute evaluation, it seemed evident that the most visual improvement occurred in those patients who were most intent in their training, putting into it more actual effort and concentration, and vice versa. It also seems pretraining acuity seemed to get the best results.

Recently Pincus has reported observations of 50,000 examinations on eyes free of organic defects and correctable to 20/20. He correlated the unaided visual acuities with the refractive errors, including myopia, hyperopia, and astigmatism, in amounts up to six diopters. All of our

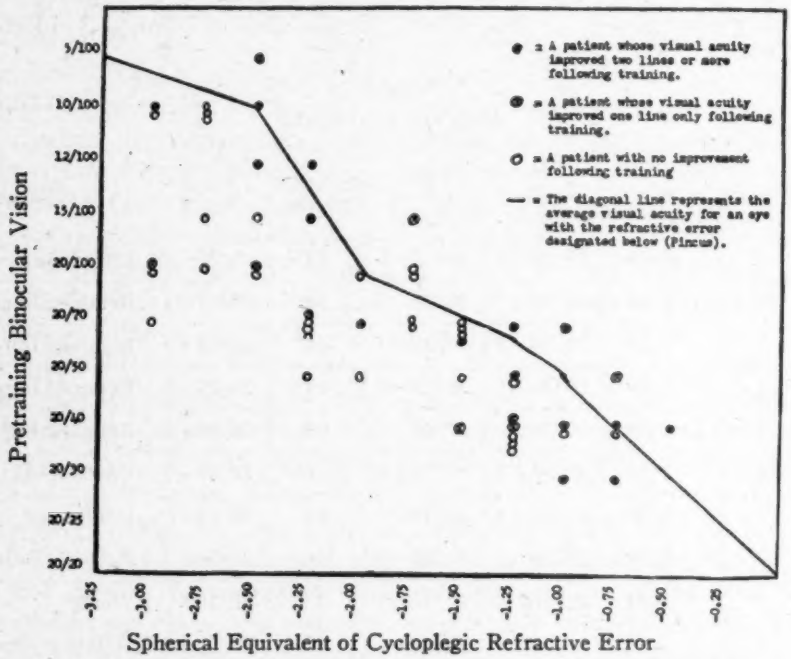

Chart 1 (Hildreth, Meinberg, *et al.*). Results obtained in visual training of existing myopia.

significant that many of the patients whose visual acuity did not change, thought that they could see better after the training. Also the subjective impression of improvement in the majority of the patients was out of proportion to the measurable change. Many stated that they thought they could "use" their eyes better.

One of us (B. M.) in analyzing the results made a significant observation that may well explain the benefit of training and may give the refractionist a criterion for selection of cases for training. It was noted that the patients with subnormal cases were grouped according to their spherical equivalent and their pretraining acuity. Using the Pincus figures as a norm, it was found that in the 11 patients with an acuity of less than expected for their refractive errors, 8 of these cases (73 percent) showed some improvement. In the 43 patients having an acuity better than expected only 16, or 37 percent, showed improvement. This is expressed graphically in Chart 1.

Realizing that our series was somewhat small, the same one of us subjected Woods' series of cases to a similar analy-

sis, using only those cases that fulfilled our limitations. Since Woods did not report binocular vision, the analysis was done on individual eyes, 110 being available. In the group with pretraining vision worse than the norm, the percentage of improvement was 76.4 percent, while in the group with better vision than the norm, improvement was 38.8 percent. This again shows the remarkable similarity between our results and those of Woods. This also definitely confirms these observations.

Since the great preponderance of improved patients were those whose acuity was not as good as was to have been expected for the amount of their myopia, we may conclude that in these there had been a failure to utilize their visual possibilities to the best advantage and that training had improved the neurologic reception of the images. Better vision is not obtained by changing the anatomy, which remains stable, but by stimulating the visual effort and by improving the interpretation of the images seen.

It is probable that similar training would, in like manner, benefit some hyperopic patients.

The results of the late reëxamination, about 1½ years after training, also may have significance. This showed that approximately one half of the patients retained their visual improvement, while only one patient showed worse than pretraining acuity. This would indicate that, at least in a small number of patients, the effect is not transitory. Although the number of patients is very small, these results suggest that an investigation of the possible relationship of visual training to the progression of myopia is indicated. This is without doubt the most important problem in myopia at present and is much more urgent than that of the improvement of visual acuity. Obviously, this question could be definitely answered only after a carefully controlled study over a period of years.

We must conclude that visual training has a definite, but limited, value in about a fourth of selected myopic patients and none in the remainder. Good effects are preponderantly in those whose vision is less than expected for their known myopia. Considering the time and effort expended by the patient, the results, both in percentage of patients improved and in the actual amount of improvement per patient, must be definitely increased if the procedure is to be generally applicable to the routine management of myopia. It would seem desirable that some efforts be made to increase the effectiveness of the present methods of visual training.

In conclusion we believe that visual training merits further study from the ophthalmologist, particularly in relation to progression in myopia. This should not be left solely to the optometrist and to the psychologist as has been almost the case in the past.

Summary

1. In an attempt to improve the visual acuity, a series of 54 selected cases of myopia was given a course of visual training which was preceded and followed by a complete ophthalmologic examination.

2. The technique of training, which was based on standard accepted procedures in this field, was given by an optometrist while the pre- and posttraining examinations were made by a group of ophthalmologists.

3. Thirty, or 55.5 percent, of the cases showed no change in their acuity, while 12, or 22.2 percent, showed a definite improvement, the best results being obtained in the cases with small amounts of myopia. Twelve patients, that is 22.2 percent, showed a change so slight as to be excluded in the results. The change in the improved group averaged 27 percent.

Eleven of the 12 improved patients were rechecked at an interval of 15 to 23 months following completion of training. Five of these retained their improvement, while only one showed worse than pretraining acuity.

4. There was no change in the refractive error, nor significant alteration in the ocular neuromuscular mechanism. It was thought that the improvement probably occurred because of an improved reception due to stimulation of the visual effort, as the best results occurred in those patients with a pretraining acuity less than would be expected from their refractive error since 73 percent of this type improved.

5. Visual training has a definite, but limited, value in some myopic patients, preponderantly in those whose vision does not correspond with their known myopia. The effectiveness of visual training must be increased if it is to be generally applicable. Visual training merits further study from the ophthalmologist particularly in relation to progress in myopia.

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The optometrists associated with this project concur fully with the above results, interpretations, and conclusions.

References

Pincus, M. H. Unaided acuities correlated with refractive errors. Amer. Jour. Ophth., 1946, v. 29, July, pp. 853-858.

Woods, A. C. Report from the Wilmer Institute on the results obtained in the treatment of myopia by visual training. Amer. Jour. Ophth., 1946, v. 29, Jan., pp. 28-57.

Snell, A. C. A Treatise on Medicolegal Ophthalmology. St. Louis, C. V. Mosby Co., 1940.

NOTES, CASES, INSTRUMENTS

EPIDERMOID CYSTS OF LACRIMAL GLAND AND CARUNCLE

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The purpose in describing in detail these two cases of epidermoid cysts is to point out the differentiating characteristics (table 1) between the ordinary sebaceous cyst, the dermoid cyst, and the epidermoid cyst of which there is a rather general misconception, since even the pathologists disagree as to the exact characteristics of these tumors.

An additional point of interest is the knowledge that according to Samuels,[1] dermoid tumors of the eye globe are relatively common; whereas, true dermoid cysts are of rare occurrence, probably being, in his opinion, rarer than intraocular retinoblastoma or sarcoma. The typical location of the cyst is in the upper temporal quadrant of the orbit near the lacrimal gland. These cysts may not be always well defined, which makes their

TABLE 1

POINTS FOR THE DIFFERENTIAL DIAGNOSIS OF SEBACEOUS, DERMOID, AND EPIDERMOID CYSTS

Sebaceous Cyst	Dermoid Cyst	Epidermoid Cyst
1. Lined with stratified squamous epithelium. Walls thin.	1. Lined with stratified epithelium. Walls thick and contain sweat glands and hair follicles.	1. Lined with stratified epithelium. Walls moderately thick.
2. Does not contain the fatty, sebaceous, and odorous material, that is typical of a sebaceous gland.	2. Invariably contains a cheesy material of a sebaceous character.	2. Contents are sebaceous but not odorous.
3. Contains layer upon layer of useless, nonfatty, odorless, infected keratin. Commonly called keratomas.	3. Contains sebaceous and sweat glands and hair follicles. The *congenital* dermoid cyst of teratoma type may encapsulate teeth, nails, glandular, and brain structure.	3. Contains no hair follicles, sebaceous or sweat glands.
4. Occur in the subcutaneous tissues of any part of the body, mostly in the scalp and in the lobe and on the posterior surface of the ear.	4. Develop along the embryonic clefts and lines of fusion. The *teratoma* type takes its origin from the embryonic germinal epithelium. Usually occur in the testes and ovaries.	4. (a) *Acquired* inclusion cysts mostly involve the orbital region and eyelids. These regions are the fusion sites of various embryonic structures. (b) *Congenital* inclusion cysts are located anywhere in the sebaceous tissues.
5. They are freely movable under the skin, although attached to the skin at one point.	5. Not freely movable. Solidly attached to the surrounding tissues.	5. *Congenital* inclusion cysts are are not attached to the overlying skin. The *acquired* inclusion cysts are the result of an injury. In the process of formation they may carry a portion of the skin into the deeper tissues where the dermal cells subsequently form a cyst lined with squamous epithelium. They occur most commonly about the head and neck.
6. Increase rapidly in size, have a tendency to become infected, and are painful. They have an enlarged pore through which exudes a cheesy material, upon local pressure.	6. May have a hair sticking out. Do not become infected.	6. Possess a sinus from which a hair may protrude. Local pressure will express a cheesy material. Enlarge rapidly and frequently become infected.

diagnosis difficult. In a number of cases, diverticula of these cysts were found to extend deep into the orbit (Knapp,[2] Gifford,[3] and Collado[4]).

The dermoid cyst tends to grow larger at the age of puberty. Depending upon its location, it may become tender and painful. Histologically, these cysts pre-

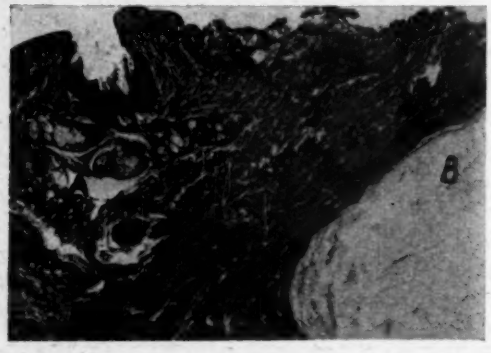

Fig. 1 (Rolett). An epidermoid cyst of the lacrimal gland. (A) Sebaceous gland. (B) Large cyst (Magnification ×56).

sent the following essential features: (1) An inner epithelial lining; (2) in the wall are imbeded hair follicles; (3) sebaceous and sweat glands; (4) the inner epithelial lining may be partly replaced by granulation tissue and, in cases of secondary infection and ulceration, may contain epithelioid and giant cells. In some cases, degenerative changes are brought about by the increased intracystic pressure due to persistent accumulation of sebum and desquamated epithelium, New,[5] and others have found that 49.5 percent of the acquired dermoids involve the orbital region and eyelids. The dermoid cysts will develop in these regions because they are the fusion sites of various embryonic structures.

Tumors of the caruncle, according to the literature, are exceedingly rare. The lacrimal caruncle and the semilunar fold take their origin from ectoderm and mesoderm. Although quite susceptible to trauma and infection, they resist the invasion of pathologic processes. Wätzold[6] found only six cases in 60,000 patients. Vail[7] saw one case in 15,000 patients, and Serra[8] compiled 136 cases from the literature, including three cases of his own.

Case reports

Case 1

P. L., a man, aged 29 years, was first seen in March, 1946, complaining of tearing and burning of the right eye with occasional sharp, shooting pain in the right upper lid. There was a feeling of fullness and a sensation of the presence of a foreign body in the right upper quadrant of the eye.

Examination. The right eye revealed a slight puffiness of the upper lid with a tenderness on deep pressure at the upper outer corner. The bulbar conjunctiva, temporally and above, was congested with enlarged blood vessels. Eversion of the lid with simultaneous extreme rotation of the eye, nasally and down, revealed a mass at the outer upper quadrant of the eye, apparently nonadherent, but painful to touch. Several hairs were seen protruding from it. The rest of the eye was normal. Vision was 20/20. The left eye showed no pathologic condition. Vision was 20/20.

An operation was performed under local anesthesia. The lacrimal gland was

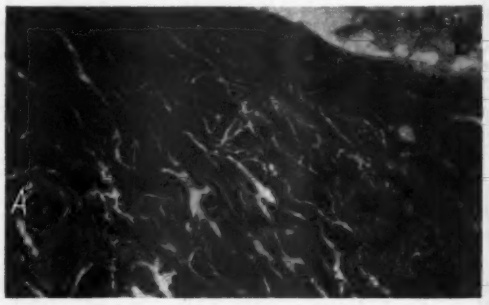

Fig. 2 (Rolett). An epidermoid cyst of the lacrimal gland. (A) Hair follicle. (B) Large cyst (Magnification ×220).

located, and a medium-sized cyst, partly overlying it and partly fused with it, was located and removed intact.

Laboratory report. Gross examination showed the specimen to consist of a soft elliptical nodule, 4 mm. in its maximum dimensions and composed of gray and yellow tissue. Zenker fixation was used.

Histologically, the tissue is composed of collagen and fat covered by a delicate stratified squamous epithelium. Included in it is a cyst lined by thinned-out stratified squamous epithelium and filled with shreds of keratin. There is no inflammatory reaction about it, but in the corium, patchy edema and scattered lymphocytes, plasma cells, and large mononuclear cells with a few polymorphonuclears are noted.

Diagnosis. Epidermoid cyst of the lacrimal gland (figs. 1 and 2).

CASE 2

C. M., a man, aged 30 years, was first seen in May, 1946, at which time the patient gave the history of having noticed in the inner corner of the left eyeball a small swelling which had become progressively larger and more painful.

Examination. The right eye appeared normal. Vision was 20/20. In the left eye, the lids were normal but the bulbar conjunctiva, nasally, was moderately congested. Through this area coursed enlarged blood vessels. The caruncle and the area around it were red. The caruncle itself was about three times the size of the one on the right side, which was normal. Palpation and slight pressure over the area elicited pain and tenderness. There was also pain on extreme motion of the eye to either side. Slitlamp examination of the area revealed an enlarged porous opening through which a thick yellowish fluid exuded on pressure. The rest of the eye was normal. Vision was 20/20.

The clinical diagnosis at the time of the examination was infected cyst of the caruncle. An operation was performed, and the cyst was removed.

Laboratory report. Gross examination of a specimen of tissue from eyelid shows a spherical cystlike structure, 3 mm. in diameter. It is covered externally by an opaque, gray, large, shiny membrane that presents a few short fibrous tags. It is fixed uncut. Zenker fixation was used.

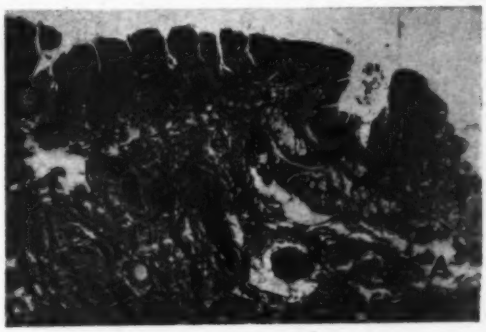

Fig. 3 (Rolett). An epidermoid cyst of the caruncle. (A) Sebaceous gland (Magnification ×56).

Histologically, the cyst has an epithelial lining made up of a thin layer of stratified squamous cells. It is filled with a quantity of keratin that is loosely arranged with spaces between the keratin layers, suggesting the presence of fluid. Outside the epithelium is a delicate fibrous wall containing a few compressed glands of modified sebaceous type.

Diagnosis. Epidermoid cyst of caruncle (fig. 3).

SUMMARY

Two rather rare cases of epidermoid cysts of the lacrimal gland and the caruncle have been presented with a description of their gross and histologic appearance. A brief review of the points of differential diagnosis between the most important cysts found in the orbit has been given.

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REFERENCES

[1] Samuels, Bernard. Dermoid cysts of the orbit. Arch. of Ophth., 1936, v. 16, Nov., pp. 776-782.
[2] Knapp, A. Arch. of Ophth., 1923, v. 52, p. 163.
[3] Gifford, H. Recurrent dermoid cyst: Successful treatment with trichloracetic acid. Arch. of Ophth., 1929, v. 2, Sept., p. 305.
[4] Collado, P. F. Rev. Med. de Barcelona, 1928, v. 9, p. 99.
[5] New, G. B., and Erich, J. B. Dermoid cysts of the head and neck. Surg., Gyn. & Obst., 1937, v. 65, pp. 48-55.
[6] Wätzold. Tumors of the lacrimal caruncle. Ztbl. f. pract. Augenh., 1913, v. 37, p. 42.
[7] Vail, D. T., Jr. Mixed tumors of the lacrimal caruncle. Arch. of Ophth., 1933, v. 10, pp. 593-601.
[8] Serra, G. M. Tumors of lacrimal caruncle: Clinical, anatomopathologic and statistical study. (Complete bibliography.) Boll d'ocul., 1928, v. 7, p. 783.

THE VITAMIN IN OPHTHALMOLOGY

It is a pleasure to recommend *Le Vitamine in Oftalmologia,* by Giambattista Bietti. (Bologna, Licinio Cappelli, Editore, 1940. 539 pages, paperbound. Price, L.80). It is a comprehensive and readable treatise on the vitamins in ophthalmology. The ophthalmologist may well bog down at the mere thought of facing a book of more than 500 long pages on the vitamins, yet here is all he wants to know so clearly stated, so perspicuously arranged, that the contemplation of the monograph is truly refreshing. After a brief general introduction, each of the five vitamins important in ophthalmology, A, B_1, B_2, C, and D is thoroughly discussed in a separate chapter. Each chapter follows the same pattern. In a general part the biochemistry of the vitamin, its relation to the normal and abnormal function of the several systems of the body, and its therapeutic indications are discussed. In an ophthalmic part, the lesions and pathologic processes in the eye in which the vitamin or its absence may play a part are thoroughly discussed. Research on incompletely elucidated problems is described. A brief chapter is devoted to the vitamins of minor interest in ophthalmology, namely E,H,J,K,L, and P.

In a final chapter the correlation among the vitamins and their relation to hormones and ferments is discussed. Each chapter has an adequate bibliography and there is a general bibliography at the end of the book. Finally, as in the condensation of Toynbee's *Study of History,* there is a condensation of the condensation. A large table displays all important data at a glance.

F. H. Haessler.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLORADO OPHTHALMOLOGICAL SOCIETY

January 18, 1947

DR. GEORGE STINE, *presiding*

DETACHMENT OF CHOROID AND RETINA

DR. GEORGE STINE read an interesting paper with a case report of this subject (published in the JOURNAL, 1947, Volume 30, July, page 987).

Discussion. Dr. Fritz Nelson offered the idea that the term choroidal detachment is really a misnomer as the condition actually is an edema of the retrochoroidal space. If a membrane detachment extends beyond the midline, it must be the retina which is detached since the vortex veins would always be ruptured with disastrous results if a choroid were detached to that extent. He had examined the patient referred to in the case report about one year after the first operation. The patient was doing very well; vision and fields were normal enough.

Dr. Stine (in closing) said that probably no more than two veins could be thus ruptured; however, there was no harm in doing a posterior sclerotomy and draining off the retrochoroidal blood.

RETROLENTAL FIBROPLASIA

DR. VON HALER BROBECK presented M. S., aged 20 months, one of premature twins who weighed two pounds at birth. The other twin died at birth. The exact gestation period was not known. The mother is a deaf mute. When first seen the child was obviously blind and had a marked nystagmus as well. Examination under anesthesia revealed large gray-white masses behind both lenses, with retinal vessels visible in the mass. A differential diagnosis would have to be between retinoblastoma and retrolental fibroplasia. The child's birth history would seem to indicate retrolental fibroplasia.

Discussion. Dr. George Stine said that he had examined the child and that he felt the condition was certainly retrolental fibroplasia; that the prognosis for vision was certainly hopeless; and that he did not recommend surgery. Dr. Ralph W. Danielson agreed and added that most of these cases also have mental retardation so that the condition might be called, "cerebro-oculo-dysplasia," although the late Dr. Terry disagreed with this idea.

TUNICA VASCULOSA LENTIS

DR. WALTER A. OHMART presented C. A., aged 17 months, who was born prematurely at six months, weighing 2 lbs. 2 oz. The child remained in an incubator for three months; it was obvious almost from birth that vision was deficient. Development was quite normal in all other ways and the child now feels its way along when walking. The pupils react easily to light and accommodation, but it is obvious that the child has light perception only. Examination shows both lenses to be clear with several anterior synechias. Both fundi present either large masses in the vitreous or large retinal detachments, involving the whole retina in the left eye and lower half in the right. The optic-nerve heads cannot be seen in either eye, and X-ray films show no calcium. Examination under transillumination has been very unsatisfactory. The diagnosis is not determined, but the condition must be bilateral serous detachment, or retinoblastoma, or tunica vasculosa lentis.

Discussion. Dr. William Bane, who had examined the child, felt this case was not one of a malignancy. Dr. W. H.

Crisp felt it was most likely tunica vasculosa lentis and felt no surgery should be done. Dr. George Stine felt that since an error might be fatal, the worse eye should be enucleated to determine the tissue diagnosis and thereby possibly save the other. Dr. Leonard Swigert suggested that the history pointed toward a benign lesion, but that since the tumor seemed to be posterior to the lens, the condition pointed to glioma. Dr. Ralph W. Danielson said that X-ray studies are not conclusive. He has a patient in whom X-ray studies showed no calcium and yet, after enucleation, the bulb was found to be almost solid. Calcium would be evidence of degeneration of the tumor and thus of the cure and not the progress of the tumor. In this case, the loose retina does not point to glioma. Since the pupils dilate to light, there is strong evidence that the condition is one of retrolental fibroplasia. A glioma of this extent could only result in blindness. He suggested that a biopsy be done. Dr. Ohmart (in closing) said that the idea of a biopsy was very good and might be attempted.

Functional amblyopia

Dr. Morris Kaplan presented L. P., aged 11 years, who has complained of poor vision for a long time. Vision was 10/400 and 6/400. The child was in fifth grade and seemed to be able to maintain average grades. Ocular examination was entirely negative and refraction under atropine revealed −3.50D. in each eye, with no appreciable improvement in vision. A history of night blindness was questionable, and there certainly was no abnormal retinal pigment. Trial contact lenses brought vision to 20/25 in each eye. Was this a case of retinitis pigmentosa without pigment; or did it show a type of hysterical functional amblyopia?

Discussion. Dr. W. H. Crisp said that if refraction revealed a simple myopia with normal retinoscopic reflexes, then conical cornea could be ruled out. Dr. William Bane said that the girl's school accomplishments would seem to indicate that no pathologic condition was present but that the condition was a purely functional ocular laziness and suggested the use of a collyrium with very stinging properties.

Iridescence of anterior chamber

Dr. R. W. Danielson presented J. C., a man, aged 21 years, who had been seen five years before immediately after a dynamite-cap explosion at which time a jagged piece of copper was removed from the sclera near the ciliary body. Subsequent X-ray pictures were negative for a foreign body. The resulting vision was 0.8. Six months later the patient suffered a vitreous hemorrhage which resulted in retinitis proliferans and vision of light perception. Three days ago his eyes became red and painful and examination revealed the anterior chamber to be solid with an iridescent mass, which was filled with variegated crystals and presented an amazing color pattern in the beam of the slitlamp. The cornea was quite clear and no reflex could be seen past the opaque lens. Tension was 28 mm. Hg (Schiøtz). His other eye has remained entirely normal.

Discussion. Dr. Leonard Swigert suggested the possibility of aspirating some of this anterior chamber material and determining its makeup.

Unusual formation of retinal vessels

Dr. W. H. Crisp presented Mrs. G. A. B., aged 55 years. When first seen, in 1931, the patient had shown great tortuosity of the retinal veins of the right eye, especially in the region of the disc, where there were several very prominent vascular loops, the highest of these having a prominence of about 5D. At that time the refraction of the right eye was nearly

normal; the visual acuity was 5/3, mostly, with correction; and the visual field was normal. There were several vague symptoms, perhaps attributable to a rather marked refractive difference between the two eyes. The retinal vessels of the left eye were somewhat tortuous, but much less so than those of the right eye. At various times between January, 1931, and May, 1938, the patient's eyes underwent moderate refractive change, but her condition showed generally very little modification. At one time some very tiny spots, probably hemorrhagic, had been noted in the retina, and the veins of the right eye showed marked kinking, but no narrowing, at the arteriovenous crossings. In June, 1938, Wassermann and tuberculin tests were negative, the blood pressure and basal metabolism were low. X-ray studies of the intracranial and facial region were negative as to pathologic conditions in the sinuses, orbit, and pituitary region, except as to the presence of a calicified pineal gland. There were some attacks of scotoma scintillans, and in October, 1938, there was some suggestion of moderate enlargement of the right blind spot. There were no other cranial symptoms such as headache, nausea, or dizziness. In September, 1939, the patient underwent a thyroidectomy. The vision of the right eye was then still 5/3, mostly, with correction.

The patient was in Washington for five years during World War II. In July, 1945, she came with the record of having noticed diminishing vision in the right eye for the past 8 or 9 months. The corrected vision at this time was: R.E., 5/6; L.E., 5/3. The psychiatrist who had examined the patient some years previously saw her again and reported finding only what he regarded as an anxiety neurosis so far as the neuropsychiatric condition was concerned.

By December, 1946, the vision of the right eye had fallen to less than 1/60, while the vision of the left eye remained as before. The visual field was limited to a small central area. The right pupil still reacted briskly to consensual stimulus, the X-ray findings were still normal, and there was no significant neurologic evidence. The vessels on the right disc were perhaps slightly less prominent than at earlier records. The optic disc between the groups of prominent vessels was very pale. In the absence of other explanation, it had been conjectured that the ocular and visual changes arose from some sort of vascular anomaly behind the eye; although there was no ocular protrusion, no limitation of movements, and no fundus details suggesting Hippel's disease or other fundus disturbances beyond those here described.

Almost no vision remained in the right eye at the time of presentation of the patient, while no disturbance was found as regards the left eye, and the patient was otherwise in good physical condition.

Discussion. Dr. V. H. Brobeck asked if this might be angiomatosis. Dr. George Stine asked the feasibility of X-ray treatment. Dr. William Bane suggested that this must be a lesion in front of the chiasm as the left vision had remained normal. Dr. Crisp (in closing) remarked that the case did not resemble angiomatosis and that X-ray therapy might be considered.

Morris Kaplan,
Secretary.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

February 20, 1947

Dr. Burton Chance, *chairman*

Paroxysmal lacrimation when eating.

Frank C. Lutman, Capt. (M.C.), A.U.S. (by invitation) read a paper on

"A Syndrome of Paroxysmal Lacrimation When Eating Associated with External Rectus Paralysis (the gusto-lacrimal reflex of 'Crocodile Tears')." An abstract follows:

Paroxysmal lacrimation when eating, which is occasionally seen as a sequel to a peripheral facial nerve paralysis upon the same side, is an abnormal form of reflex in which tearing accompanies salivation. The explanation for the abnormal facial movements following peripheral facial motor paralysis and other pathologic associated reflexes is also applicable here. From all cases now available, the evidence would suggest that this reflex tearing is established by either some of the regenerated axones to the salivary glands becoming misdirected to the lacrimal gland, or that single axones at the point of the lesion may branch and innervate both the lacrimal and salivary glands. However, the center for this reflex, if peripheral, remains obscure.

Two cases were described. The first was a congenital unilateral paroxysmal lacrimation when eating with a homolateral paralysis of the external rectus muscle. The second had bilateral external rectus paralysis and bilateral reflex tearing when eating. Upon reviewing the literature on lacrimation when eating, a third and similar bilateral case was found. In all three cases the condition was first noticed in infancy.

It is suggested that the pathologic processes in these three instances is produced by a pontine lesion, involving the abducens nucleus and the superior salivary nucleus of the seventh nerve, or by a lesion of the abducens nucleus and the genu internum of the facial nerve as it passes around the abducens nucleus.

The three cases of paroxysmal lacrimation when eating associated with external rectus paralysis are presented as evidence of the existence of a new congenital neuro-ophthalmologic syndrome.

For treatment, if the reflex tearing can be interrupted by cocainization of the sphenopalatine ganglion, injection with alcohol offers a more permanent means of control. When indicated, the external rectus paralysis should be treated by tendon transplants from the superior and inferior recti muscles.

Discussion. Dr. Robert A. Groff: Captain Lutman has presented a rather interesting and new syndrome, so far as I am aware, when he adds to the familiar paroxysmal lacrimation during chewing movements, a homolateral external rectus paralysis.

I became interested in the syndrome without the external rectus palsy some 6 or 7 years ago when I saw a patient who teared whenever he ate an apple. This patient gave a history of having had a facial palsy from which he had completely recovered some 8 or 10 months before. As Captain Lutman suggested in the treatment of this condition, we, at that time, injected the sphenopalatine ganglion and produced temporary cessation of the phenomenon during the time the novocaine was acting. Since this was successful, the second injection was made with ½ to 1 cc. of absolute alcohol, and for a period of about three months the patient was symptom free. After that he disappeared from the clinic, which may indicate that the difficulty did not return.

As to the association of the syndrome with a sixth-nerve palsy, rather than a facial palsy, I have had no personal experience. This is new, although I say it with hesitancy since I have not reviewed the literature. My reaction to Captain Lutman's explanation that this is caused by a central lesion is not in agreement. Certainly, the associated tearing with seventh-nerve lesions has been more or less proved to be a peripheral reflex phenomenon. The possible pathways are chordatympanic nerve, sphenopalatine ganglion, and then through the zygomatic

nerves to the lacrimal gland. It may be that in some way the fifth cranial nerve is involved, in view of the studies that Dr. Lewey and I carried out in connection with the Marcus Gunn phenomenon in which we demonstrated autonomic fibers in the branches of the fifth nerve which, when stimulated, caused eyelid movements after the third cranial nerve had been sectioned several weeks before. For this reason and because a central lesion would necessarily have to be minutely small to produce this syndrome without giving other neurologic signs, the entire phenomenon could better be explained on the basis of a peripheral perversion reflex. Furthermore, the fact that relief was obtained by injection of the sphenopalatine ganglion tends to support this view.

I wish to thank Captain Lutman for the privilege of discussing this interesting presentation.

Dr. Walter I. Lillie: I would just like to assure Captain Lutman that he has been fortunate in seeing so many cases because they are very rare indeed. I was very much interested as I have only seen one case with an external rectus paralysis and lacrimation. I feel as Dr. Groff does that it is a peripheral lesion. I personally do not see how one could conclude that there is pontine reaction in the region of the sixth nucleus where the seventh knees around it. The pons is a very small portion of the central nervous system. A lesion large enough to include the seventh nerve kneeing around the sixth nerve plus the salivary center produces a lot of contralateral motor and sensory disturbances in the individual, and that to my knowledge has not occurred. I think Dr. Lutman is to be congratulated on seeing as many cases as he has.

Capt. Frank C. Lutman (closing): With Dr. Lillie and Dr. Groff I also believe this is a peripheral reflex. A lesion of the pontine facial nucleus would produce a peripheral facial paralysis which as I brought out in the paper is a requisite for this type of paroxysmal lacrimation to develop. As I understand Dr. Groff's contention, it would require two lesions to explain a combination of the abducens paralysis and the facial paralysis. To my mind it would be simpler to attribute this to a single lesion, and the point where the facial and sixth nerves are the closest together is in the pons.

However, as has been mentioned, this tearing is rather complicated, and I hope in the future a careful neurologic examination will be done in the new cases that are found.

I wish to thank Dr. Groff and Dr. Lillie for discussing the paper.

Meningeal fibroblastoma arising from sphenoid bone

Dr. Robert H. Trueman, presented an analysis from an ophthalmic point of view of the syndrome of meningeal fibroblastoma arising from the lesser wing of the sphenoid bone.

The historical aspects of suprasellar and parasellar meningiomas were considered with particular emphasis on the early observations of those arising from the sphenoid ridge.

The terms suprasellar and parasellar were defined, with a description of the sphenoid ridge. The anatomy of the region of the lesser wing of the sphenoid bone and sella turcica is reviewed and the pathology of meningioma was discussed.

The syndrome of early meningioma of the lesser wing presents such findings as optic atrophy, field changes, exophthalmos, involvement of ocular motility, sensory disturbances in the distribution of the second and first divisions of the trigeminal nerve, involvement of taste and smell, all on the side of the tumor. The appearance of pituitary and frontal lobe and motor and sensory symptoms and signs were also discussed.

The symptomatology of 56 cases was

analyzed to show that in 82 percent of them the first symptoms to appear were of an ocular character. The objective findings were then analyzed to show that 91 percent of the cases showed fundus changes, 86 percent showed visual field changes, 43 percent showed exophthalmos, and 38 percent showed some involvment of ocular motility. Among the findings, other than ocular, were trigeminal parethesias, pituitary signs, involvement of taste and smell, frontal lobe signs, sensory and motor findings.

The X-ray findings were then discussed with particular reference to both generalized and localized changes among which are the erosions and the local and general hyperostoses.

The differential diagnosis was taken up in relation to intraorbital tumors, intrasellar tumors, aneurysms, optochiasmic arachnoiditis, gliomas, and craniopharyngiomas.

Discussion. Dr. Robert A. Groff: Dr. Trueman is to be congratulated upon his excellent presentation. Certainly, he has clarified the syndrome since Dr. B. J. Alpers and I first called attention to it some years ago.

The successful surgical removal of these tumors depends upon early diagnosis, because then the technical problem is simplified greatly. The lesion is small and, as a result, the opportunity for complete removal is much more favorable.

The picture presented to you includes cases of late diagnosis. In fact, some of them were made at a time when it was not possible for the surgeon to operate upon them. Let me give you the early signs which are sufficient to make the diagnosis. Early primary optic atrophy of papilledema, a visual field cut on the temporal side of the affected eye, and a top normal sella turcica are all that is necessary to demand further studies to verify the diagnosis by encephalography.

When a unilateral exophthalmos is developing in a patient, the possibility of a sphenoid lesser wing meningioma should be excluded first. X-ray films of the skull will aid in the diagnosis for, in my experience, the ridge shows definite thickening incident to tumor infiltration.

At the operation these tumors are interesting. They present either one of two types. The first is a bulbous growth, and the second is an en-plaque variety in which the tumor is flat, spreading over the surface of the dura. This latter type is usually associated with underlying bone infiltration which produces exophthalmos.

In order to cure these patients, it is necessary to remove the dura to which these tumors are attached. The bulbous variety offers a less difficult problem, from this stand point, than those which grow by spreading over the surface of the dura. The former, therefore, if not large can usually be removed completely. The latter are almost never removed completely and, therefore, recur. Since this type of tumor is a rather slow grower it is, in most instances, several years before a second operation is necessary.

When the bone has been invaded by the tumor, it is practically impossible to remove all of the involved bone because of the adjacent structures, internal carotid artery, nasal chamber, and sinuses and sphenoid fissure. Although a routine decompression of the orbit is done in those patients who have an exophthalmos, it does not relieve this sign completely but only partially.

Dr. Trueman stated that the cause for the exophthalmos is probably venous engorgement. As one observes the orbital contents in these patients, this explanation seems most likely, because the structures are edematous and under tension as though there was obstruction to the venous drainage system of the orbit.

A plea is made for the early recognition of these tumors. As Dr. Trueman has

stressed in his paper, when a patient comes to you with a slight primary optic atrophy, a temporal field defect in the same eye, and the X-ray pictures of the pituitary fossa are normal or top normal in size, have him investigated for the possibility of a lesser wing sphenoid ridge tumor without delay.

I wish to thank Dr. Trueman for the privilege of discussing his excellent presentation.

Dr. Walter I. Lillie: I would like to add my appreciation for Dr. Trueman's presentation, and to go one step further in what he has called the early part of the ocular syndrome.

The early thing is the retrobulbar neuritis syndrome on the side of the lesion. That is characterized by a lowering of the visual acuity. The visual fields will usually show a central scotoma, although they may have otherwise normal findings. This is the ideal time for the diagnosis to be made as it permits the neurosurgeon to enter and remove the tumor before it has been of long enough duration to have produced optic atrophy. Optic atrophy is irreversible, a condition which I wish to stress even stronger than Dr. Groff did.

The ophthalmologist sees these cases first, and he is the one responsible if they are delayed in reaching the neuro-surgeon. In the early stages there is usually a normal fundus, and it is necessary to differentiate the lesion from an inflammatory type of condition or a toxic thing. Against that type of clinical syndrome, the onset of this, as Dr. Trueman has brought out and Dr. Groff has also stressed, is very insidious, and it progresses slowly. This indicates tumor rather than inflammation or vascular lesion. I feel that in these cases a very thorough neurologic examination is necessary, and should be requested by the ophthalmologist. I also strongly advocate doing an encephalogram early. I believe that this is helpful in basal arachnoiditis in the sulcus chiasmatis, in lesions of the sphenoidal ridge, and in calcification. If it shows a massive type of space-taking lesion, it is a great aid. I concur with both speakers, but I feel that it should be stressed to take heed of the earliest eye syndrome and not to wait for the appearance of optic atrophy. If a case can be operated before atrophy has taken place, that patient has a very excellent chance to recover normal vision and that is the ideal end result.

Dr. Burton Chance was reminded by this history of a case of his own. He had been consulted by a lawyer who was engaged in a suit concerning the death of a woman after the collision of the automobile in which she was riding with her family, and a horsedrawn vehicle. Photographs made by bystanders absolutely confirmed the transportation company's contention that the company was not at fault, nevertheless a verdict was entered against the company.

Before the injured one's death it was declared that her sight had been destroyed, and that she was blind. Dr. Chance succeeded in obtaining the record books of an ophthalmologist, then deceased, who, 11 years before the accident, had been consulted by the woman. He recorded that she was blind in her right eye, because of complete atrophy of the optic disc, which he regarded as dependent on the high degree of progressive myopia of each eye. At that time there were no roentgen facilities, and further study was not made. Against the opposition of the plaintiff's family, an autopsy was obtained. Attached to the sphenoid was found a tumor of about the size of a large white grape extending by erosion into the orbit. Sandlike changes were felt over the surface of the tumor. By some strange sleight-of-hand the tumor was spirited away, and was never recovered!

Dr. Robert H. Trueman (closing):

Thank you, Dr. Groff and Dr. Lillie, for your discussions. You have both emphasized, as I have tried, the importance of the early changes in the diagnosis of this tumor.

I would like to call attention to the fact that this analysis includes cases representing all sizes of these tumors from the largest, in the early Cushing series, to the smallest in the series of Groff and Elsberg, and Dyke. This explains the varied types of clinical pictures found, from the very early fundus and field changes to bilateral blindness. While it is important to recognize the very early changes, one should know that, as the tumor grows, progressive changes occur, for it is possible that a case might just as well be seen late as early.

I would like to ask Dr. Lillie one question. In your experience, have you ever been able to pick up a case of meningioma of the lesser wing that had only a central scotoma?

Dr. Lillie: Yes, I have.

Dr. Trueman: That answers my question. Thank you.

Night vision for military personnel

Robert H. Peckham, Ph.D., associate professor Physiological Optics, Department of Ophthalmology, Temple University Medical School (by invitation) presented a paper on "The Protection and Maintenance of Night Vision for Military Personnel."

This address is a report of the recommendations and research performed by the Vision Committee of the National Defense Research Committee for the military services during the war. The author acted as liaison officer between the Committee and the Bureau of Medicine and Surgery.

As a result of the deliberations of this group of civilian and uniformed scientists, the following action was undertaken by both the Army and the Navy.

1. All personnel were instructed in the use of the eyes at night, with especial attention to waiting for dark adaptation and to using the rods of the retina by "looking around things."

2. An attempt was made to supply night-combat personnel with red goggles, to preserve dark adaptation, and to permit the attainment of adaptation in lighted compartments.

3. All Navy personnel were examined to eliminate night-blind persons.

4. As a result of directed research, it was decided that sunglasses for day wear were necessary to permit the best night vision. These sunglasses were neutral in color, not green or amber, of 10-percent transmission, and polarized, with the plane of transmission vertical. Finally, no specification against transmission in either ultraviolet or infrared was included.

5. The facts learned during the war can be applied to peacetime pursuits. Since the effect of sunlight is to reduce the sensitivity of the retina, sunglass protection is recommended for fluoroscopists. The effect of sunlight is to reduce the efficiency by about 30 percent. Sunglasses are needed by all persons doing colorimetry, or any visual task involving comparative judgment. The effect of sunlight reduces retinal efficiency by from 20 to 50 percent, depending on the task.

In a determination of avitaminosis by measuring the course of dark adaptation, the effect of previous exposure to sunlight could conceivably be so great as to completely confuse the readings. Sunlight exposure can be effective for as long as three weeks after the period of exposure, and the effect of vitamin therapy can, therefore, be lost to demonstration.

All persons driving in dusk and at night, after a day in unprotected sunlight, will lose at least one half of their night visual efficiency, thereby rendering their driving dangerous and uncertain.

Discussion. Dr. Burton Chance, in commenting on the statement that persons exposed for long hours in the glaring sunlight were found to have distinct loss of power at night, remarked that he had noticed on his repeated visits to tropical islands that his native friends seldom would enjoy walking out with him at night, because they declared they could not see well at night.

On long voyages, as once on a sailing ship before he became an ophthalmologist, he noted how sailors, who had been most capable during the daylight hours, became less efficient during the night, especially after the periods when their daytime watches were prolonged.

In World War I, at his Army Hospital located at the seaside, men from northwestern climates who delighted in spending all the daylight hours on the beach would prefer to remain indoors at night. Dr. Chance believed that the daylight glare interfered with the photochemical reactions in the retina.

Dr. Walter I. Lillie: I would like to have a word before Dr. Peckham's closing remarks. We have read so much in the newspapers that the Negro race, the yellow race, and the brown race have much better night vision than the white race. I just wondered whether any of his investigations would prove or disprove those statements?

Dr. Robert Peckham (closing): We made a lot of measurements designed to distinguish racial differences. The first measurements were made by the Army for the purpose of selecting drivers of trucks and jeeps under blackout conditions at Fort Meyers. They deliberately chose members of the Negro race, because it was suspected that, being highly pigmented, they would have deeper choroidal pigmentation and be better able to see at night. The tests showed no difference. Many more careful and extensive tests were made during the war until it was finally concluded that no one race showed any superiority of retinal sensitivity.

Some races were better able to perform out of doors at night, being better trained for night vision, because of their savage environment. At one time early in the investigations, we received a hurry up call from the British that the suggestion had been made that the Japanese were night blind. Because they were myopic, something ought to be the matter with them. Fortunately, a few retinal sensitivity records of Japanese students were available, but these showed no differences in retinal sensitivity.

During the Pacific campaign the Marines reported hearing Japanese broadcasts to the effect that the American Marines should stay indoors at night. It was proported that certain selected Japanese Shinto fighters had been selected for retinal operations, including the injection of secret drugs, and were then trained to be night killers. These people, it was boasted, had such tremendous retinal sensitivity that they could not go out of doors in the daytime, and therefore would not be seen. This sounded like a fairy tale, but it had to be investigated. It was concluded that it was in reality a falsehood, invented by the Japanese, because they had discovered that they had actually lost their night retinal sensitivity. They had occupied the islands for months, and even years, waiting and watching for us to come. They were aware of their night-vision loss, because we found their foxholes literally lined with boxes of vitamin-A concentrates. We had ourselves tried the use of such concentrates, and found that they were useless to replace lost retinal sensitivity. Only time, and considerable time at that, will permit the retina to regain its lost sensitivity.

George F. J. Kelly,
Clerk.

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THE STUDY OF OCULAR MOTILITY

The members of the American Board of Ophthalmology are in a unique position to compare and evaluate the training of ophthalmologists from all over the country. There is, of course, the uniformity of the topics taught and examined in, as set forth by the prospectus of the Board. Naturally, too, there is a wide variation in the assimilation of the necessary knowledge and techniques of ophthalmology by the candidates. The Board members have a very good idea of what institutions and preceptors turn out the best product. The quality of the teaching and opportunities is reflected in the standing of the candidates as a rule, although there are many exceptions.

Among the subjects that cause some

confusion and express the most variations in training throughout the country is that of ocular motility. This, however, should occasion no surprise because at the moment the leaders and teachers, themselves, are somewhat confused over the subject, which is inherently difficult to comprehend in all of its complexities. There is a modest conflict between investigators of the objective method of examination and diagnosis, as exemplified by Duane, White, and many others, and the followers of the neuromuscular and subjective method of examination and interpretation, as represented by Bielschowsky, Lancaster, Burian, and Adler.

The contributions of Duane and White have been important and helpful in the understanding and measurement of squint. The fact that it is a method of objective measurement with screen and prism has the fault that, in following this method, there is a tendency for one to discount or overlook the associated disturbed physiology or anatomic lesions in the ocular muscles or central nervous system underlying the objective signs. Adler brought this out very well in his Jackson Memorial Lecture, recently presented before the American Academy of Ophthalmology and Otolaryngology, when he discussed the "underaction" phenomenon in the nonfixing, nonparetic eye.

On the other hand the contributions of the neuromuscular school are probably more comprehensive and accurate, although more complex. The method of charting diplopia fields, advocated by the authorities, is not easy and the interpretation of these diplopia fields is certainly not automatic. Lancaster's chart with red and green goggles and targets simplifies the diplopia test and comes close to making it a satisfactory objective method of measurement and analysis. It needs a patient who is reasonably intelligent and who understands what is required of him.

Perhaps most of the candidates at the last examination of the Board followed more or less the objective method of measurement. Many had what has been lightly termed "P. trouble" or prism trouble, or "F.F.P." (fist full of prisms), and the usual difficulty of a fixation light and not enough hands was frequently encountered. Few were at home with diplopia tests, and while many showed some knowledge of the work of the neuromuscular school from their study and reading, not many had considered this side of the story intently.

The student suffers from lack of clear writing and description of both methods; especially the neuromuscular one, in our modern textbooks. The Duane-White method is only to be found in a few of the new textbooks on ophthalmology, and the neuromuscular method in this event is given scanty mention. The manual, *The Extrinsic Eye Muscles,* of the Home Study Course of the American Academy of Ophthalmology and Otolaryngology, prepared by H. Saul Sugar, covers both features of this somewhat thorny subject pretty well. There is, however, a need for a good and clear treatise. That this need is obvious is shown by the experience of the Board examination.

In view of the present and laudable state of controversy, no one method is entirely satisfactory in all cases or for all examiners. It would seem best, therefore, for the beginner to master the objective method first and then deeply study the "neuromuscular" methods until he has mastered them in so far as possible. In this way the best features of both methods will be preserved and followed, and a better interpretation of the patient's ocular muscle imbalance will result. Better and more complete methods of analysis will insure a more accurate diagnosis and will naturally result in better treatment.

Derrick Vail.

BOOK REVIEWS

OPHTHALMOLOGY, BEING SECTION XII OF EXCERPTA MEDICA. Amsterdam, The Netherlands. Excerpta Medica, Ltd. Price, $15 per year.

A new abstract journal has been launched whose purpose it is to publish a complete survey of the entire medical literature. This is to be accomplished by 3,000 specialists who work under the supervision of 400 editors. One may subscribe for any number of the 15 sections which are published separately.

The first issue of Section XII, Ophthalmology, has been received. The preface states that completeness is the first objective the editors have set for themselves. Abstracts of articles of any importance will be at least long enough so that the reader may judge for himself whether he wants to refer to the original. When it is impossible to give a detailed abstract, the title will be given to draw the reader's attention to the existence of the original. The second objective is to produce a readable text for those readers who cannot find time to cover the world literature of their specialty in the original.

The coverage seems to be complete. The section on ophthalmology compares favorably with the prewar *Centralblatt*. There are 48 pages of competently written abstracts, all by men of the highest caliber. The abstracts, all in English, are so comprehensive that the general reader is adequately informed, and the investigator of a similar problem can judge whether he needs to consult the original. Not only are the major ophthalmic articles abstracted, but articles of ophthalmic interest are taken from journals which most specialists would not think of combing. Most of the publications abstracted in the first issue appeared in 1946, a few as early as 1940. The preponderance of articles from 1946 justifies the belief that abstracts will appear rather promptly.

It is perhaps inevitable that the general reader who uses this journal as a substitute for the original literature will find himself exhausted. Such concentrated diet engenders a state comparable to museum fatigue. The material is, after all, a collection of condensations made by many men and presumably not altered by one editor in the interests of unity of viewpoint. It is not the function of an editor to evaluate critically the data presented by the original author, but he can be of tremendous help to the general reader by pointing out, often with the utmost brevity, the significance of data which the original author presents with comments that are only adequate for a fellow-worker but cryptic for the general reader.

F. H. Haessler.

RETINAL STRUCTURE AND COLOUR VISION. By E. N. Willmer, Sc.D. Cambridge, University Press, 1946. 231 pages, 77 illustrations (4 in color), index, and bibliography. Price, $4.50.

This monograph presents a novel, stimulating, and plausible theory of retinal function. The increasing interest in this little understood field should lead to further research to test its validity and implications. Willmer's thesis, in simplified outline, is this:

The central fovea is dichromatic when precisely tested with 20-minute test objects. The color confusions that result from the relative insensibility to blue are typical of tritanopia. This sensitivity of the fovea to but two color factors simplifies the analysis of the mechanisms involved. The bipolar cells of this area include not only the midget type, characteristic of the direct-cone pathway, but also

flat bipolars, typical of a rod-cone pathway. Hence the deduction: that the fovea has receptors belonging to the rod family of cells, dependent on visual purple for their spectral sensitivity, though incapable of the rapid accumulation of visual purple necessary for dark adaptation. The cone-midget bipolar unit is then the "red receptor," while the "green receptor" is formed by the combined action of cones and nonadapting rods relaying centrally through the flat bipolars.

The perception of blue appears connected with the normal rod-mop bipolar pathway, for in blue light acuity is higher in the retinal periphery than in the fovea. Since light adaptation increases the sensitivity to blue, the light-adapted rod, which has experienced some bleaching of visual purple, may be considered the "blue receptor." This view is supported by the interrelationship of tritanopia and night-blindness, the sensitivity to dim light in tritanopia being about 0.55 percent of normal. A 5-mm. blue disc only appears full blue when the object approaches near enough for the image to involve the parafovea.

Inhibition of the adapting rods by the cones, suggested by the electroretinogram, reduces rod activity during daylight and prevents dazzle. Rod-cone antagonism may be likened to that of the sympathetic and parasympathetic systems. From the nature of their dendrites and the action of drugs, the cones would seem cholinergic and the rods adrenergic.

When the energy values in the scotopic and photopic visibility curves are related to impulse frequency, the results reasonably explain the characteristics of the color chart, hue steps, and color variations at different light intensities and by addition of white. In this respect the application of Willmer's theory gives significance and coherence to what has hitherto seemed inexplicably bizarre.

In birds, color vision probably depends on three types of cones, but there is no such evidence in man. Willmer's interpretation, though admittedly speculative, has the advantage of being based on what has been already demonstrated in human visual physiology. A possible mission of the Eye Banks could be the further advance of our knowledge in this field by the procurement of eyes of known types of color blindness for the study of their retinal structure and photochemistry by especially qualified investigators—a direct approach, previously unfeasible, that promises much.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology

1

GENERAL METHODS OF DIAGNOSIS

Jaques, R. **The size of the blind spot in aphakic eyes.** Ophthalmologica, 1947, v. 113, June, pp. 365-374.

The author measured the horizontal and vertical diameter of the blind spot in 27 emmetropic and 29 aphakic eyes. Campimetry with lenses correcting the aphakia proved difficult and unsatisfactory apparently because the strong lenses produced marked and inconsistent distortion of the perimetric findings. The author, therefore, resorted to campimetry without correcting lenses, using a round white fixation target two centimeters in diameter. The size of the blind spot was determined at one meter with a white target one centimeter in diameter, moved from the seeing into the blind area. Under these conditions, the normal blind spot of the aphakic eye proved to be about one-third larger than that of the emmetropic eye. This empirical result tallies with the theoretical one, since the refractive power of the emmetropic eye (58.64D after Gullstrand) is about 1.35 times the refractive power of the aphakic eye (43.05D). Peter C. Kronfeld.

Vaško, A., and Peleska, M. **Visual diagnosis of eye diseases by means of infrared radiation.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 419-421.

In their studies the authors illuminated the eye with infrared radiation of a wave length exceeding 8,500 Å. The image was then projected by means of an objective lens onto the photoelectric cathode of an image converter. This converter transformed the infrared image into a visable image on a fluorescent screen. This image on the screen was then photographed.

Morris Kaplan.

2

THERAPEUTICS AND OPERATIONS

Andrews, G. W. S. **Distribution of penicillin in the eye after subconjunctival injection.** Lancet, 1947, v. 1, May 3, pp. 594-596.

Subconjunctival injections of 50,000 units of pure sodium penicillin were made in the left eyes of four rabbits.

The bleb was absorbed at the end of three hours and the eyeball appeared normal at the end of six hours. The blood serum contained four units per cc. in one half hour and reached zero at the end of two hours. The concentration in the aqueous reached 16 units per cc. in one half hour and fell to one unit per cc. at the end of four hours. The cornea contained 170 units per cc. one half hour after the injection and fell to 1.7 units per cc. at the end of four hours. The levels in the optic nerve were high, but fell rapidly. The uninjected fellow eye had a similar distribution, but with lower levels of concentration. Irwin E. Gaynon.

Angius, T. and Mojne, G. **Plesiotherapy (contact radiation) in ophthalmology.** Rassegna Ital. d'Ottal., 1947, v. 16, March-April, pp. 107-130.

The authors report upon 91 cases of various pathological conditions of the eye, especially corneal disease, treated by contact doses of roentgen radiation. Small doses were especially effective in herpes of the cornea and subacute, torpid keratitis with decreased corneal sensitivity. The treatment should be applied as early as possible and dosage should never exceed 400 r. The treatment is interrupted as soon as improvement is observed, even after one application, lest re-activation of the disease should occur. Eugene M. Blake.

Apple, Carl. **Instruments for use in ophthalmic surgical procedures.** Arch. of Ophth., 1947, v. 37, May, p. 652.

The author's corneal scissors are a modification of the Walker scissors. The lower tip extends 1 mm. beyond the upper tip; the extended part is 1 mm. wide; the extreme end is rounded, and the surface is highly polished. This enables the operator to enter the anterior chamber with less difficulty and without trauma to the iris after the original section of the cornea.

In the iris redepositor described, the handle may be rounded or square; the round handle enables the operator to rotate it between the thumb and the index finger. The redepositor portion is bent at an angle of 115 degrees and is 5 mm. long and 2 mm. wide; the extreme end is rounded and dull, and the surface is highly polished. (2 figures.) R. W. Danielson.

Bellows, J. C., Burkholder, M. M., and Farmer, C. J. **Streptomycin in experimental ocular infections.** Proc. Soc. Exper. Biol. and Med., 1947, v. 65, May pp. 17-18.

On rabbits anesthetized with intravenous injection of nembutal the penetrability of streptomycin through the cornea is increased by abrasion, inflammation, ion transfer and wetting agents. No local toxic effects were noted when saline solutions of streptomycin containing 10,000 ug per cc., were used. Concentrations of 50,000 ug or the dry powder caused delayed healing. Intraocular injections of 1,000 ug in 0.1 cc. saline solution were well tolerated. Concentrations of 25 to 300 ug were therapeutically effective (up to 6 to 8 hours) against a virulent strain of Streptococcus pyogenes. Corneal ulcers were prevented in Bacillus pyocyaneus infection by three applications at two-hour intervals of a saline solution containing 10,000 ug of streptomycin per cc. H. C. Weinberg.

Benedict, W. L., and Henderson, J. W. **Sodium sulfacetimide.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 984-986. (9 references.)

Bonazzi, A. **Surface anesthesia with Farmocaine.** Rassegna Ital. d'Ottal., 1947, v. 16, May-June, pp. 224-227.

Farmocaine is a new surface anesthetic presented by the firm of Farmitalia. Employed in solutions varying in strength from one-fourth to 2 percent the drug produces rapid anesthesia, with no effect upon the intraocular pressure, pupillary diameter, or the epithelium. It is of low toxicity and boiling it for 10 minutes at 100 degrees C. does not destroy its action.

Eugene M. Blake.

Esente, Ivan. **First therapeutic experiments with paraaminobenzoildiethylaminoaethanol chloride (Recorcain) used intravenously in ocular diseases.** Riv. di Oftalm., 1946, v. 1, Nov.-Dec., pp. 671-678.

Recorcaine was first used in 1941 by Dos Ghali, Bourdin and Guiot. One percent solutions were given intravenously in asthma, pulmonary embolism, and angina syndromes, dyspnea of emphysema, and tuberculosis. With and without additional atropine administration, the drug proved to be useful in gastric neuroses and gastric ulcers, it was used in carbon monoxide poisoning and in hyperthermic coma. The drug acts as a depressor of the respiratory center which, with higher dosage, may become paralyzed. Muscular contractions become rarer, the action on peripheral nerve centers is inhibitory. An antihistaminic action was ascribed to the drug by State and Wangensteen, 1946. Through the vegetative centers the drug produces a transient heat sensation and slight drowsiness, or sleep. Ocular pain and headache are relieved for shorter or longer periods. Lutton, Roumer, Giraud and Ferran were able to combat eclamptic amaurosis by intravenous administration of recorcaine. Esente used it in painful glaucomas, where the results mostly were satisfactory (no statistics). Pain was relieved and intraocular pressure was reduced for much longer than the time during which the drug was administered. Simultaneous use of miotics may enhance these effects. The doses given varied between 10 and 100 centigrams.

K. W. Ascher.

Filatov, V. P. **Problems of tissue therapy.** Oftal. Jour. (Odessa), 1946, pt. 3, pp. 1-6.

The experience and research with tissue therapy during the war eliminated the chief objection to this method of therapy, that is, the lack of sterility in transplanted tissue. It was found that the therapeutic effect of tissues preserved on ice is not diminished by boiling, and by autoclaving at 120 degrees for one hour. This fact was demonstrated experimentally by Skorodinskaja and Tarasova in restoring skin defects on white mice, and clinically in such diseases as myopic chorioretinitis, uveitis, and trachomatous pannus. Inasmuch as in boiled extracts albumens are present only in insignificant amounts, heterogenous tissues may be used without fear of anaphylactic reactions. The effectiveness of extracts of green leaves, preserved in darkness, further simplified this form of therapy in making possible their administration orally or by rectum. The value of this form of therapy has been demonstrated in hundreds of cases of trachoma, where it was used in combination with repeated expression. Tuberculous, parenchymatous, herpetic, and trachomatous keratitis react to this therapy very well. It is of value in traumatic uveitis and vitreous opacities. It constitutes the chief therapy in retinitis pig-

mentosa. It is useful in all types of optic atrophy, and in glaucoma. An incidental effect is the improved function of the uninvolved eye. It has proved valuable in a number of general diseases such as experimental tuberculosis in animals, lupus, scleroderma, neuritis, neurodermatitis, and posttraumatic contractures and limitation of movement. During the war this therapy was used and found effective in ulcers of the stomach, in lesions of the peripheral nervous system, in epilepsy, in typhus, brucellosis, pellagra, and leprosy. On the basis of experimental and clinical investigations the following hypothesis is presented. Tissues separated from the organism and subjected to an atmosphere unfavorable to life undergo biochemical changes; as a result of these changes they produce substances which stimulate the biological processes. These substances, when introduced into an organism, act as stimulants of its biologic processes; they stimulate cellular metabolism, and thus physiologic functions; in case of disease they augment the organism's regenerative powers and resistance to disease. Biogenic stimulants, products of biochemical changes, arise also in organisms placed in environments which make life difficult, but not impossible; such a reaction may play a role in the process of evolution. The crisis in acute infections is an example of unfavorable conditions leading to biochemical changes with the development of stimulators. Conditions leading to the development of biogenic stimulators are varied; preservation of animal tissues on ice, preservation of plants in darkness, the action of ultraviolet light, exposures to X ray and fever therapy. Biogenic stimulators are the products not of the dead cell, but of the living cell fighting for life. It has been shown in botany that traumatized cells produce traumatic acid, belonging to the dicarbon group. It is possible that the biogenic stimulators are of a similar nature. Since they tolerate a high temperature they could not be albumens or ferments. This hypothesis may explain the beneficial effect of mud therapy, which Filatov believes is due to the biogenic stimulators accumulated in the mud by the living substances which took part in its formation. Autoclaved extracts of seashore mud prepared at the Institute produced effects similar to those of tissue extracts. Agricultural experiments have shown that preliminary processing of seeds of corn, wheat, and oats with extracts of preserved tissues hastens their sprouting, ripening, and productiveness. Ray K. Daily.

Haffly, G. N., and Jensen, C. D. F. **Method for the maintenance of sterility of ophthalmic solutions.** Arch. of Ophth., 1947, v. 37, May, pp. 649-650.

The authors use 20-cc. rubber-capped vaccine bottles for their ophthalmic solutions. The rubber cork is painted with zephiran chloride before each removal of solution with a syringe and needle.

R. W. Danielson.

Halbron, P., and Aitoff, H. **Nylon thread in ocular surgery.** Ann. d'Ocul., 1947, v. 180, March, pp. 158-167.

The relative advantages of absorbable and nonabsorbable sutures are discussed in detail. Ocular sutures should be resistant, easily manipulated, have a smooth surface, should not swell, should not produce inflammatory reactions and should be easily sterilized. The form of nylon currently used for suture material is polyheamethylene adipamide. It has a density of about

1.5, a refractive index of 1.55, its molecular weight varies between 10,000 and 20,000, it is not affected by ordinary temperatures or the usual solvents, equally resists alkalies and diluted acids, and has a resistance to traction which is superior to silk. Multibrin, a braided nylon, is more supple, is more adequately knotted and has an elasticity superior to natural silk. Nylon sutures are better tolerated by the tissues than silk; no reaction has been observed after three weeks. The sizes usually employed are 0.1-mm, 0.15-mm, 0.2-mm. Sterilization may be accomplished by wet heat or dry. In cataract extractions a 0.15-mm. thread is used in the superior rectus for fixation, and in conjunctival and corneo-scleral suturing. Knots should be firmly tied because the material is slightly elastic. Corneo-scleral sutures fall out about the tenth day. In muscle operations the 0.15-mm. or 0.2-mm. sizes are used and should not be cut too short. In eviscerations, or retinal detachments the 0.15-mm. sizes may be used. In skin sutures, nylon is of special value because of its size and because it slides easily in the tissues. (13 references.)

Chas. A. Bahn.

Owens, E. U., and Woods, A. C. **The use of furmethide in comparison with picocarpine and eserine for the treatment of glaucoma.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 995-996. (1 table, 2 references.)

Palomino Dena, Feliciano. **Problems and recent advances in ocular surgery.** Anales de la Soc. Mexicana de Oft., 1947, v. 21, April-June, pp. 88-107.

This is a brief review of a number of recent papers on ocular surgery, including the subjects of pterygium, corneal transplant, intracapsular cataract operation, retinal detachment, and other details. (Bibliography.)

W. H. Crisp.

Puglisi-Duranti, G. **Vaccine-therapy (spirochetic vaccine of Hilgermann) in some cases of ocular syphilis.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 407-420.

Hilgermann vaccine is prepared from strains of nonvirulent polivalent spirochetes and is used together with chemotherapy to secure sterilization of the system and to prevent the late nervous manifestations. The writer treated seven patients, two of whom had anterior uveitis, four optic neuritis, and one total paralysis of the third cranial nerve, with varying degrees of success. The treatment is to be tried in neuro-ophthalmic syphilis which very frequently is a forerunner or concomitant of grave forms of neurosyphilis.

Melchiore Lombardo.

Quilliam, J. P. **Di-isopropylfluorophosphonate (DFP); its pharmacology and its therapeutic uses in glaucoma and myasthenia gravis.** Post-Grad. M. J., 1947, v. 23, June, pp. 280-282.

Aqueous solutions of DFP are unstable because of hydrolysis. DFP combines irreversibly with choline esterase. Choline esterase activity is restored when the enzyme protein is resynthesised. Peanut oil is used as a vehicle. In the normal eye DFP may cause miosis that lasts three weeks with ciliary spasm for three to seven days. It overcomes atropine easily. In glaucomatous eyes, a 0.1 percent solution, is effective for 12 hours. A 0.1 percent solution of DFP is as effective as 1 percent esserine.

Irwin E. Gaynon.

Schubert, Franz. **The effect of iodine baths on diseases of the eye.** Wiener

Klin. Wchnschr., 1947, v. 59, July 4, pp. 435-436.

The author who practices in Bad Hall, Austria, reports his favorable experiences in treating certain eye diseases of patients who took the cure in this community which harbors springs containing iodine. Tuberculous inflammations like keratoconjunctivitis excematosa and chronic tuberculous iritis showed marked improvement. The progress of chorioretinitic lesions could be stopped with subsequent improvement of the visual acuity. The bath-cure hastens the absorption of vitreous opacities, especially those caused by hemorrhages. The large group of arteriosclerotic diseases which lead to retinal hemorrhages and to retinal degeneration responds favorably to an extensive iodine cure. So do cases of partial venous thrombosis. Interstitial luetic keratitis improved under the treatment. The article emphasizes the necessity of repeated annual visits. It is not made clear how the water is administered nor how it is believed to act.

Max Hirschfelder.

Thomas, G. J., and McCaslin, M. F. **Pentothal sodium in ophthalmic surgery.** Arch. of Ophth., 1947, v. 37, April, pp. 452-458.

Pentothal sodium by intravenous injection is an important anesthetic for ophthalmic surgery. The administration is simple, the induction is short and pleasant, the depth of narcosis is controllable, the operative field is free of the anesthetist and his equipment and the intraocular tension is reduced 40 to 60 percent.

Pre-anesthetic medication consists of the administration of morphine and atropine and the local use of cocaine. The technique of administration and the complications are discussed. Pentothal sodium should not be employed if there is pronounced interference with the respiratory function, if there is bronchiectasis, severe anemia or shock and its use is not advisable in children under seven or eight years of age. The drug should be administered by a thoroughly trained anesthetist, who is competent to deal with any situation that may occur. John C. Long.

Vidal, F., Brodsky, M., and Travi, O. C. **Miosis due to carbaminoylcholine in patients with retinal angiosclerosis.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Oct.-Nov., p. 350.

In 31 cases of retinal angiosclerosis the instillation over the corneal limbus of one drop of a 0.33 percent solution of carbaminoylcholine chloride produced a miosis. It began in about five minutes as in normal individuals but reached its maximum in 30 minutes and lasted longer than in normal eyes. (Bibliography.) Plinio Montalván.

Vidal, F., and Villa, E. **Practical modifications of the Schiötz tonometer.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Oct.-Nov., p. 313.

The authors modified the Schiötz tonometer by substituting two threaded bolts for the screw that holds the disc of the plunger, painting red and black the markings of the scale, and attaching two cupped discs for the fingers when holding the instrument. (Illustrations and bibliography.)

Plinio Montalván.

Vidal, F., and Zappi, D. A. **Imperfections of tonometers of the Schiötz model.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Oct.-Nov., p. 325.

Fourteen Schiötz tonometers of Austrian, American, French, German and Swedish manufacture were tested

with a modified torsion scale and all of them were found to be inaccurate. (Bibliography.) Plinio Montalván.

Vouters, J. **Basal scopolamine-morphine-ephedrine anesthesia in ophthalmology.** Ann. d'Ocul., 1947, v. 180, March, pp. 149-157.

S-M-E anesthesia is recommended in major ophthalmic operations in nervous patients especially if immobility of the eye is important, as in glaucoma and cataract surgery, and in infants. It is useful in some enucleations, eviscerations, and operations for intraocular foreign body, in operations of long duration such as retinal detachments, lid plastics, orbital exenteration, and in dacryocystorhinostomy.

One hour before operation two cc. of a French proprietary drug called Nargenol is injected subcutaneously. This solution contains dihydroösycodeinone 2.00, scopolamine camphosulfonate .0005 ephedrine camphosulfonate .002, spartine .005, and physiological salt solution q.s. ad. 2.00. In infants, one fifth cc. is injected and in a child of five years, one cc. is used. The advantages of this type of anesthesia are that it leaves a clear field for surgery, the period of anesthesia is reduced and there is no agitation nor vomiting. Occasionally slight respiratory irregularity may appear 45 minutes after injection, which can be overcome by caffeine or lobeliene. Under certain conditions the anesthetic solution may be increased to four cc. without danger. Barbiturates and bromides tend to accentuate its effect. Chas. A. Bahn.

3

PHYSIOLOGIC OPTICS, REFRACTION, AND COLOR VISION

Albada, L. E. W. **Construction of the paraxial images and the path of a ray through an optical system.** Acta. Ophth., 1947, v. 25, pt. 1, pp. 1-8.

This is a mathematical demonstration. (7 geometric figures.)

Ray K. Daily.

Arjona, J., **Stenopeic hole and its use.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 425-435.

The stenopeic hole has a number of uses in ophthalmology, some of which are practical and others experimental. Its principal clinical use is to distinguish between the low vision of a refractive error and disturbances of the transparent media, retina or optic pathway. The basis of its action is a reduction to a minimum of the circles of diffusion on the retina. These circles are larger the higher the degree of ametropia. The stenopeic hole may be used as a loupe for viewing near objects for the same reason. To avoid movements of the eye the hole is used after operations for retinal detachment. Its use has been recommended for albinos.

It also has experimental uses. In Mile's experiment, when a distant light is seen through the stenopeic hole, which is moved forward to the anterior focal plane, one of three things may occur. The light remains fixed, it moves in the same direction as the hole, or in the opposite direction. In the first case the eye is emmetropic, myopic in the second and hypermetropic in the third. This experiment was the basis of the kinescopy, wherein the movement of the light is neutralized by means of lenses. In Scheiner's experiment two stenopeic holes are placed horizontally in a screen less than a pupillary diameter apart. When a pin is viewed through the two holes while the eye fixates a nearer object the pin is seen

double and diplopia is direct. When the eye fixates a more distant object diplopia is crossed. This experiment proves the existence of accommodation and is used to measure its amplitude. Several diagrams are shown for the better understanding of these experiments.

J. Wesley McKinney.

Burian, H. M. **The place of peripheral fusion in orthoptics.** Amer. Jour. Ophth. 1947, v. 30, August, pp. 1005-1010. (3 references.)

Burian, H. M. **Sensorial retinal relationship in concomitant strabismus.** Arch. of Ophth., 1947, v. 37, May, pp. 618-648.

In this portion of a paper too long to print in one issue of the Archives, the author discusses the origin, literature and nomenclature of anomalous correspondence. This is an excellent paper for those who are interested in this subject and already understand some of the fundamentals. Any abstract would be inadequate. (106 references, 9 figures, 2 tables.) R. W. Danielson.

Carreras Matas, B. **A concept of the degree of myopia and hypermetropia in an astigmatic eye.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 348-350.

As a formula for the measure of myopia or hyperopia of an astigmatic eye Matas uses the sum of the diopters of sphere and half the diopters of astigmatism. He demonstrates the mathematical derivation of this formula.

Ray K. Daily.

Gallagher, J. R., Ludvigh, E. J., and Martin, S. F., and Gallagher, C. D. **Effect of training methods on color vision.** Arch. of Ophth., 1947, v. 37, May, pp. 572-582.

In various surveys it has been found that from six to eight percent of unselected males are unable to make the proper responses to a series of color vision test plates. Regardless of the reliability of various testing methods or the desirability of altering present standards, there still remains the problem whether the color vision of those who fail to pass these tests can be modified. Whenever large numbers of persons are excluded either from a branch of the armed services or from a civilian occupation because of a physical disability, there will develop a demand from those affected that the disability be remedied or that the standards applying to it be lowered. In the problem at hand, the rejection of many otherwise well-qualified men has led to efforts to improve the color vision of these rejectees so that subsequently they might be able to pass the color vision tests. In an effort to determine the effect of training methods, a group of subjects previously identified as being deficient in color vision was studied.

Forty-nine subjects who had been selected as weak in color vision on the basis of responses to the American Optical Company pseudo-isochromatic test plates were subsequently given training on those test plates until all but 4 could satisfactorily pass that particular color vision test. However, only 6 made perfect responses to all the plates in the very similar Ishihara test, and the scores on a color desaturation test, which also had not been practiced, did not improve. A retest on the American Optical Company plates several months later showed a considerable diminution in ability to make correct responses to these plates and indicated

that the effects of this type of training may not long persist.

Color vision training apparently is successful in enabling most persons with weak color vision to respond correctly to such a test as the American Optical Company plates or the desaturation test herein described, but from this study there is no evidence that either of the training methods used improved the capacity to discriminate between colors in a situation other than the one in which training was given. (6 tables, 2 figures, 6 references.)

R. W. Danielson.

Gát, L. **A new subjective test for astigmatism.** Ophthalmologica, 1947, v. 113, Feb., pp. 93-105.

A dial test for astigmatism has been combined with Scheiner's double pinhole test for ametropia. The dial recommended by the author consists of a heavy, black, double cross, the strokes of which are two centimeters wide and placed two centimeters apart. In the center the strokes are interrupted except for four black squares (two centimeters square) at the actual crossing places of the horizontal and vertical strokes. These central squares apparently facilitate the observation of the various distortion phenomena due to astigmatism. The dial can be rotated around the axis laid through the center of the cross. It is viewed through a double pinhole (1-mm. holes, placed 2.5 mm. apart). Ametropia causes diplopia which, because of the construction of the dial, is easily noticed and described. The author stresses the accuracy of the method. "It is possible to find axis divergence of 2° and astigmatic ametropia of 0.25D." The test requires "comparatively little intelligence and power of observation."

Peter C. Kronfeld.

Giudice, Mario del. **Ocular allergy.** Rev. Brasileira de Oft., 1947, v. 5, June, pp. 209-218.

In various parts of Brazil, where the tree is native, and also in India, where it is cultivated, the natives make a household remedy for infestation by lice by grinding the seeds of the first of one of the anonaceae, Rollinia sylvatica, and mixing it with pork fat. The mixture is rubbed into the hairy scalp and the hair is subsequently washed with soap and water. The author reports several cases of allergic reaction in the eyelids and conjunctiva, with abundant tearing, slight mucous secretion, intense photophobia, burning, and itching. Alleviation may be obtained from instillation of adrenalin solution. (One illustration, references.)

W. H. Crisp.

Hartmann, E. **The psychology of vision.** Ann. d'Ocul., 1947, v. 180, April, pp. 193-205.

Hartmann presents a brief but comprehensive analysis of the mental aspects of the process of vision. We seldom see what we think we see. Retinal images differ greatly from visual interpretations. The latter are composed of our proprioceptive stimuli, intellectual concepts, past experience, and hereditary factors. One may ignore or eliminate parts of the pattern of visual perception, as is done by one with strabismus or in using the microscope. We may add to our visual perceptions as in viewing cartoons. Personalities such as Li'l Abner or Jiggs, are in reality only a few printed strokes and devoid of detail.

In the perception of colors our sense of values is modified by the surroundings of the object perceived. Psychologically, we associate colors in an orthodox manner. We know that violet

is a red-blue but we do not realize red as violet-orange. The same is true of complementary colors. We also associate color values with emotional values. Red suggests the rich, sumptuous, or gay; violet, the majestic; black, sadness; certain greens, outdoor life. The association of red with heat or warmth, blue with cold, is used in the color schemes of homes and factories.

In the concept of form, visual interpretation plays an important part. In the steps of Schroeder or the cube of Necker the third dimension of depth, which does not exist on the retina, is added by our imagination. Knowing that money is round, our consciousness does not register the many ellipses that are actually formed when discs are viewed at different angles.

Our interpretation of direction depends on numerous factors. The actual retinal image, our visual fields as related to parts of our body, as well as our proprioceptive sensations which emanate from the muscles of our eyes, neck and trunk, all enter into this complex visual function.

In estimating the size of objects we are guided by the macular and peripheral image sensation, combined with angulation. A small object in the sky may be first recognized as an airplane but soon it is known to be a gull.

The estimation of distance involves not only our central and peripheral retinal visual sensation, but also our judgment gained through past experience, and color differences such as zones of shadow or the bluish color of the air. Paralactic displacement and linear perspective also enter into this complex mental process. After years of blindness those who have regained sight have at first a very poor sense of distance.

Reversal of the inverted picture on the retina does not actually exist as the visual perceptions involved are really reversed in the calcarine region. Rapidly moving objects when photographed show a blurred course which does not exist in vision. Binocular single vision is obtained by merging the two retinal images to give the inference of depth. If the monocular components are identical, the binocular perception does not differ from the two components. If slightly different, the binocular perception is intermediate; but if the monocular components differ too widely, binocular perception is impossible, and one of the images is either neutralized, or both images strive for supremacy. In the stereoscope a false conception of depth is obtained by viewing two slightly dissimilar images through convex prisms, base in, which relaxes the accommodation and convergence. In reading, the adept does not recognize letters, or even words, individually but assembles them into groups, five or six to the line. Chas. A. Bahn.

Mata, Pedro. **A Case of erythropsia.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 436-441.

For about two weeks a boy, 10 years old, had noticed that everything became red for about a minute several times a day. During the attack the patient closed the eyes so strongly that a marked blepharospasm was produced. The vision, fundus, and visual fields were normal. All the laboratory tests were negative. The erythropsia was attributed to vascular spasm of the Silvian and posterior cerebral arteries, which produced irritative hallucinations of the optic pathway or cerebral cortex. J. Wesley McKinney.

Miles, P. W. **Clinic for binocular problems.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1169-1171.

Pascal, J. I. **Ophthalmic calculations by the "dam" method.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 424-426.

Mathematical formulas for the calculation of lens surface power of all thin and of most thick lenses are briefly presented. The "dam formula is the general formula for surface power and is properly written as D = AM. D is the power in diopters, A is the difference between the index of refraction of the second medium and the first, and M is the curvature in metrecs. (A metrec is the unit of curvature and is the ration of lens power expressed in its focal length and its radius of curvature). Thus, to estimate the power of the anterior surface of a cornea having a radius of 8 mm. and an index of 1.376 the formula is applied: $D = A\ (1.376 - 1 = 0.376) \times \frac{1000 \text{ mm.}}{8 \text{ mm.}} = 47$. Or to estimate the D of the posterior surface of a cornea having a radius of 6.8 and the index of the aqueous is 1.336: $D = 1.336 - 1.376 \times \frac{1000}{6.8} = -5.88$. The same formula applies to contact lenses and also to thick spectacle lenses where the sum of the powers of the two surfaces becomes the power of the lens.

Morris Kaplan.

Pfister, A. **A chart for the objective determination of the visual acuity.** Ophthalmologica, 1947, v. 113, June, pp. 344-364.

For a number of years H. Goldmann (Ophthalmologica, 105:240, 1943) and Pfister have been engaged in studies of the optokinetic nystagmus as a means of estimating the true visual acuity (the minimum separabile) in malingerers. Pfister now describes the many "complications" encountered and the final method evolved as the result of those complications. The cessation of the optokinetic nystagmus upon reduction of the nystagmus-eliciting pattern below the minimum separabile is the principle of the method. The moment of cessation of the nystagmus is determined by observation of a large episcleral vessel with the ophthalmoscope and a +10D lens. The examinee who is given no information concerning the nature of the test, is asked to look at a checkerboard, black and white pattern, which describes rhythmic up and down movements against a gray background. If the movements of the pattern elicit a definite vertical pendulum nystagmus, the moving checkerboard is moved farther away from the examinee until the nystagmus stops. The refractive error must be accurately corrected with glasses. The observation with the ophthalmoscope must be conducted in such a way that no light falls into the pupil and that there is no interference with the patient's viewing the chart. The aphakic eye does not lend itself to this test because of its low depth of focus. In a few perfectly normal, emmetropic (non-malingering) individuals the nystagmus could not be elicited. There is surprisingly good correlation between the subjective and the objective visual acuity in patients who admit their true acuity.

Peter C. Kronfeld.

Pignalosa, G. **Three cases of spasm of accommodation during lactation.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 415-420.

Three cases of visual disturbances in lactating women are reported in detail. General and local treatment cured the condition in a short time. The writer reviews the literature. He found that no case has been reported in which spasm

was dependent on lactation. The writer believes that in his patients anemia and a nervous depressive state were predisposing causes aggravated by the debilitating effect of lactation. (Bibliography.) Melchiore Lombardo.

Rios Sasiain, Manuel. **Some advances in physiologic optics.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 351-359.

The author reviews the newer investigations on accommodation, nocturnal myopia, double function of the retina, Purkinje's phenomenon, electroretinography, and visual substances, such as visual purple, visual yellow, and the visual cone substance.

Ray K. Daily.

Rosso, S. **The estrogens and accommodation.** Rassegna Ital. d'Ottal., 1947, v. 16, March-April, pp. 98-106.

Rosso shows by case reports that estrogens employed in the treatment of female genital disturbances lead to a diminution of accommodation. The effect is apparently due to a disturbance of the neuro-vegetative system.

Eugene M. Blake.

Safar, K. **Chalazion and astigmatism.** Wien. Klin. Wchnschr., 1947, v. 58, July 25, pp. 484.

The fact that chalazion in the upper lid may be a cause of considerable astigmatism does not seem to be well known, at least it is not mentioned in the Kurzes Handbuch. To call attention to its occurrence the author reports an astigmatism of 1 D. that was caused by chalazion. (4 references.)

F. H. Haessler.

Schmidtke, R. L. **Wetting agents for contact lenses.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 1013-1014.

Sebas, S. R. **Considerations as to astigmatism.** Rev. Brasileira de Oft., 1947, v. 5, June, pp. 221-229.

The author lays great stress on the measurement of corneal astigmatism with the ophthalmometer. He has frequently found it necessary to make separate astigmatic measurements for distant and near vision. W. H. Crisp.

Sloane, A. E. **Refraction clinic.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 1014-1016. (1 figure.)

Thomson, L. C. **Binocular summation within the nervous pathways on the pupillary light reflex.** J. Physiol., 1947, v. 106, March 15, pp. 59-65.

It has been shown that the degree of constriction of the pupil which results from the stimulation by light of the retina of a single eye was significantly less than that obtained when both eyes were stimulated.

This binocular summation was equivalent to that obtained by increasing the area of the stimulating flash between two and four times and observing with a single eye throughout.

This binocular summation does not appear to be influenced by cerebral cortical activity. The position of the summation within the nervous pathways is discussed.

Theodore M. Shapira.

Tirelli, G. **High hypermetropia.** Rassegna Ital. d'Ottal., 1947, v. 16, March-April, pp. 85-92.

Tirelli reviews the literature concerning high degrees of hypermetropia and reports the case of a six-year-old boy who had 16 diopters in the right eye and 17 in the left. The partially corrected vision was 2/10 in the right and 1/10 in the left eye. Ophthalmoscopically the only changes observed were

pseudo-neuritis and slight tortuosity of the retinal vessels. Eugene M. Blake.

Wald, George. **The chemical evolution of vision,** The Harvey Lectures, 1945-1946, Series 41, pp. 117-160.

The chemical evolution of vision is traced by the use of the knowledge that carotenoids play a major part in photoreception in plants and animals. The light stimulus, which causes molds and higher plants to bend and show other orientation, is absorbed by carotenes and xanthophylls. These pigments with another carotenoid astaxanthin, are found at the eye spots of certain green flagellates.

Arthropods and molluscs have image forming eyes but cannot synthesize carotenoids, and photoreception is dependent upon vitamin A_1 and retinene$_1$. Fresh water vertebrates (or animals that spawn in fresh water) have the porphyropsin system of the rods based on vitamine A_2 and retinene$_2$.

Euryhaline fish (which as adults can tolerate fresh water or salt water) possess both the rhodopsin and porphyropsin systems. The amphibia also have both the rhodopsin and poryphyropsin systems. The bullfrog during metamorphosis transfers from the porphyropsin to the rhodopsin system.

Iodopsin is found in vertebrate cones. It is a carotenoid-protein closely related to the rod photopigments. From the human macula a pigment xanthophyll has been isolated, showing that human foveal vision depends on an intact carotenoid. (13 figures.) H. C. Weinberg.

4

OCULAR MOVEMENTS

Anderson, J. Ringland. **Ocular vertical deviations.** Brit. Jour. Ophth., 1947, Monograph Supplement XII.

This monograph presents a study of vertically-acting ocular muscles and includes statistics on a series of 402 patients with horizontal and vertical defects of concomitant and paralytic types. The literature is reviewed. Methods of complete examination are fully described. It is emphasized that the coordinated movements of the eyes, and the compensatory movements of the head must be carefully studied. Only an exact diagnosis with accurate interpretation can lead to the correct treatment.

For the measurement of diplopia and the primary and secondary deviations the screen test is recommended. Anomalies of the vertical rotators, especially the inferior oblique are found more frequently than is usually recognized. In concomitant convergent strabismus an overacting inferior oblique muscle was present in over 30 percent, and in an additional 25 percent, paresis of at least one superior muscle was present. Combined with the horizontal defects these figures show that there are few cases of simple concomitant strabismus.

The vertical range of fusion is small and both poorly controlled and little used; thus a small vertical error readily becomes a tropia. Examination usually reveals a paresis or overaction in a vertical imbalance. It is important to distinguish between primary overactions and secondary overactions in vertical rotator pareses. Palsies of the vertical rotators are complete in that there is no response to cortical, subcortical, vestibular or other stimuli. In supranuclear ocular palsies the fibers are often affected by disease as they pass through the brain stem.

Frequent causes of ocular paresis are twilight sleep, obstetrical forceps, and

motor vehicle accidents. Recovery is the rule, although it is somewhat less for vertical than for horizontal palsies. Orthoptic training may play an important part in the treatment.

In the surgical treatment of vertical disorders three principles of correction are considered. These are the strengthening of the paretic muscle, weakening of the overacting contralateral synergist, and weakening the contracture of the ipsilateral antagonist. Vertical defects associated with concomitant strabismus may decrease or cease after the horizontal deviation has been corrected.

The author voices a need for the reporting of the results of exact findings in large series of cases to remove contradictory opinions from the literature. (37 illustrations.) O. H. Ellis.

Dering, S. A. **Post-contusion ophthalmohyperkinesis.** Oftal. Jour. (Odessa), 1946, pt. 3, pp. 40-42.

In some patients with a history of brain contusion Dering noticed a pronounced convergence, without other visual disturbances, which lasted during the period of examination, and disappeared as the examination was concluded. Two patients had a spasm of convergence, which produced a myopia of four diopters in one eye, and eight in the other, associated with transitory spasm of convergence and blephrospasm. The neurologic diagnosis in these two cases was chronic posttraumatic encephalitis, with muscle spasm. Persistent blephrospasm was another symptom frequently encountered in this group of patients. These symptoms are attributed to an irritation of the nuclei of the third nerve in the floor of the aqueduct of Sylvius, producing an involuntary, abnormal tonic or clonic contraction of the innervated muscles. Ray K. Daily.

Fink, W. H. **Anatomical variations in the attachment of the oblique muscles of the eyeball.** Trans. Amer. Acad. Ophth., 1947, May-June, pp. 500-513.

Surgery of the oblique muscles is the least understood and least standardized portion of ocular muscle surgery. This is partly due to normal and abnormal variation of insertion and size of the oblique muscle tendons. In this study of 100 specimens, variations, especially of the tendon, are described in detail. The inferior oblique shows greater anatomical uniformity than the superior oblique. Pareses, contractions and spasms of these muscles are frequently confused with anatomical variations. It is important to note the closer nasal insertion of the superior rectus in reattaching it in surgery involving the underlying superior oblique. As an anatomical landmark the overlying superior rectus tendon is preferable to the trochlear process of the superior oblique. Variations in the fascial sheath which connects the inferior oblique and the inferior rectus (ligament of Lockwood) frequently determine the results of oblique muscular surgery. The inferior oblique is best operated upon at its insertion rather than at its bony origin. The posterior edge of the insertion of the inferior oblique extends to within two millimeters of the optic nerve; as it is usually muscular and has a very short tendon, and it should be severed as close as possible to the eyeball. In the reattachment of severed muscles two sutures rather than one should be used to create as broad a line of contact as possible, and the direction of muscle fibers should not be altered.

In high myopia the position of the inferior oblique is more posterior.

Chas. A. Bahn.

Heinonen, Oscar. **Birth injury as a cause of strabismus.** Acta Ophth., 1947, v. 25, pt. 1, pp. 19-28.

The investigation was based on the study of 84 cases of strabismus, in patients whose parturition histories were available in the hospital where they were born, 75 cases in patients whose histories were obtained from their parents, and 29 cases from an institution for feeble-minded. This material is analyzed with reference to the weight at birth, abnormal fetal positions, surgical procedures for delivery, prolonged parturition, the number of first-born infants and of twins, frequency of feeblemindedness, symptoms of trauma in the newborn, and diseases of childhood. Because of the great mortality of infants with severe birth trauma or born prematurely a history of these facts is encountered in only about 10 percent of patients with strabismus. The author has the general impression however that mild birth injuries are an important factor in the etiology of strabismus, and that a history of strabismus in the family and of a difficult parturition are frequently encountered together. It is probable that birth trauma is the exogenous factor that is effective in the presence of the hereditary factor, as in other cerebral lesions. Two brief histories of strabismus in twins are reported, to illustrate the two etiological types of strabismus. In one pair of twins with intermittent strabismus, hyperopia and astigmatism, there was a history of strabismus in the family, and of a prolonged spontaneous parturition. Here the etiology is considered chiefly endogenous. The other twins had convergent strabismus with emmetropia, a history of a difficult parturition, but no family history of strabismus; here the strabismus is attributed to the birth trauma.

Ray K. Daily.

Henderson, J. W. **Optokinetic and other factors modifying vestibular nystagmus.** Arch. of Ophth. 1947, v. 37, April, pp. 459-471.

Vestibular postrotational nystagmus is capable of modification by optokinetic nystagmus. In most cases postrotational response is abolished by repeated daily rotation. This suggests that cortical influences are dominant over those of the vestibular level. There appears to be a poststimulus persistence of optokinetic rotational nystagmus which is effective in reducing postrotational response.

Variability of response has been shown to be the expected finding in the higher forms which possess a well differentiated cerebral cortex. This tends to render less valid work which has been done in lower species whose response is mainly reflex in type. This also supports the accumulating mass of evidence which invalidates the Bárány test as a precise diagnostic aid.

John C. Long.

Joly, J. P. **Considerations on the "myocampter." Hypocorrection and hypercorrection in strabismus.** Arch. d'Opht., 1947, v. 7, no. 1, pp. 51-59.

The author discusses muscle-shortening procedures, particularly tucking procedures, and describes his use of the "myocampter" and clamp. He advocates complete tenotomy guarded by suture which is adjusted postoperatively according to the state of the correction. He advocates hypocorrection for convergent strabismus with amblyopia,

and hypercorrection for divergent strabismus with amblyopia, the latter because of the natural tendency of an amblyopic eye to diverge. He has entirely abandoned the operation of advancement. Phillips Thygeson.

Kramer, M. E. **The orthoptic treatment of the vertical motor anomalies.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1113-1123. (1 table, 1 figure, 16 references.)

Márquez, M. **Physiologic explanation of the law of Hering in connection with double innervation of the internal rectus muscle of the eye.** Anales de la Soc. Mexicana de Oft., 1947, v. 5, Jan.-March, pp. 3-12.

With three excellent diagrams, the author restates, somewhat revised, his views with regard to conjugate and disjunctive movements of convergence and divergence. He postulates double innervation of the internal rectus muscle both for convergence in association with the internal rectus of the other eye and for adduction associated with the external rectus of the other eye. He confirms Hering's law of equal innervation for the two eyes for each class of movements. (References.)

W. H. Crisp.

Prangen, A. deH. **Some observations on the surgical treatment of the extraocular muscles.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1161-1168. (16 references.)

Rigg, J. P. **Operative technic for external and internal strabismus.** J. Internat. Coll. Surgeons, 1947, v. 10, Jan.-Feb., pp. 63-71.

After a brief review of the principles of the physiology of binocular coordination and a description of some of the surgical procedures for the relief of strabismus, the author describes his own operation, the advanced tuck. By means of a suture passed through the tendon of a lateral rectus muscle 6 mm. behind its insertion, this part of the tendon can be advanced to the limbus and anchored there. The tendon has been folded on itself and an additional suture through the junction of muscle and tendon is placed for scleral anchorage. A Tucker or a Berens tendon forcepts is used in the folding of the tendon. F. H. Haessler.

Rose, A. T., and Pritzker, S. **Paralysis of the abducens nerve following spinal anesthesia.** New England J. Med., 1947, v. 237, July 10, pp. 52.

A case of unilateral paralysis of the abducens nerve after spinal anesthesia is reported. Recovery was practically complete in three weeks. The onset of symptoms varies from three to 21 days and is usually preceded by headache, dizziness, stiff neck and photophobia. The paralysis is usually bilateral and is accompanied by diplopia. Recovery takes place in a few weeks or months and is usually complete.

F. H. Haessler.

Savitsky, N., and Winkelman, N. W. **Cogwheel phenomenon of the eyes; its clinical significance.** Arch. Neurol. and Psychiat., 1947, v. 57, March, pp. 362-368.

The authors state that the occurrence of the cogwheel phenomenon during pursuit movements of the eyes is abnormal, and that its presence indicates the existence of organic disease of the brain. It has been seen most strikingly with chronic encephalitis and other organic diseases.

The authors have observed the cogwheel phenomenon of the eyes with diphenylhydantoin and bromide poisoning.

The phenomenon has proved of diagnostic value especially in atypical cases of chronic encephalitis and in cases of head injuries. Theodore M. Shapira.

Sheppard, E. W. **Discussion of Miss Kramer's paper.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1124-1127. (3 figures.)

Soria. **Marcus Gunn phenomenon and voluntary nystagmus.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 325-334.

Soria reports the case of a 26-year-old man with a left-sided partial ptosis, a Marcus-Gunn phenomenon, and voluntary nystagmus. The nystagmus was horizontal, rapid, of moderate amplitude, and not exceeding forty seconds in duration; the patient initiated it by looking down. The literature on both of these rare phenomena is reviewed. Of the various theories proposed to explain the Marcus-Gunn syndrome, Soria accepts that of Marquez, who believes that the phenomenon represents an exaggerated form of normal syngerism between the movements of the mouth and the lids. He sides with Weekers in attributing the genesis of voluntary nystagmus to a cortical excitation, rather than to a cortical inhibition, as is believed by Wilbrand. (5 illustrations.) Ray K. Daily.

Swan, K. C. **Esotropia following occlusion.** Arch. of Ophth., 1947, v. 37, April, pp. 444-451.

Four cases of esotropia that developed during periods of monocular occlusion are reported. It seems that spontaneous recovery of single binocular vision is not to be expected from this uncommon, but serious, complication of a commonly used procedure. Treatment should be immediate; otherwise, the deviation tends to increase and the amplitude of fusional movements to decrease, and suppression is likely to develop.

A latent convergent tendency seems to be the condition underlying development of esotropia from occlusion; therefore, in the presence of esophoria or uncorrected hyperopia prolonged monocular occlusion for diagnostic or therapeutic purposes should be used with caution. In the reported four cases, a damage suit was instituted in three. In the treatment of unilateral amblyopia in patients with single binocular vision, lacquering the spectacle lens to reduce visual acuity in the better eye is suggested as safer than total occlusion because binocular vision is maintained. John C. Long.

Wolff, E., and Hefferman. **A note on the position of the eye in a third nerve palsy.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 427-428.

This very brief case report is presented to call attention to the fact that in oculomotor nerve paresis, the eye looks directly to the side because of overaction of the external rectus and not outward and downward. The superior oblique muscle is unable to depress the eye in extreme abduction.

Morris Kaplan.

5

CONJUNCTIVA

Alagna, Gaspare, and Faraone, Giuseppe. **Development of subconjunctival hemorrhages.** Riv. di Oftalm., 1946, v. 1, Nov.-Dec., pp. 657-670.

Extravasations of blood in the skin show color changes different from those observed on subconjunctival hemorrhages; 23 patients were studied to explain this difference. Five of them had hemorrhage with trauma, in six the cause was unknown, and in 12 the hemorrhage was experimentally induced by subconjunctival injection of one to two blood droplets of the patients own blood drawn immediately before the experiment. In this latter group, the blood deposit appeared dark red in the center, and pink in its periphery where biomicroscopy revealed irregularly distributed red cell groups. Twenty-four hours later, the diameter of the blood deposit was greater than after the injection, and biomicroscopically fine absorption lines become visible, forming a network of subepithelial radial channels, the conjunctival lymph vessels. After two and three days, the blood patch was still somewhat larger, pink in color and its borders hazy. At that time, yellowish lines were visible along the vessels, particularly the veins, easier to see at the periphery of the blood deposit. Later on, the color of the blood differs according to the location of the deposit. If it is situated in the exposed area of the bulbar conjunctiva, it changes from pink to yellow and in or near the fornix the color turns from pink to greenish. On the third and fourth day, the blood cells show changes in shape when examined with the corneal microscope and finally only granules of a yellowish red color remain. After 20 and more days, brownish granules are found near the vessel walls. In the two other groups, of traumatic and spontaneous hemorrhages, similar observations were made. The traumatic hemorrhages seemed to spread more rapidly, tortuosities and partial interruptions of vessels were seen, aneurysmatic dilatations were found in some capillaries, and a granulated current with occasional "emptying" of the capillaries was observed.

The injection of blood under the conjunctiva of each eye of two dogs followed by closure of the lids of one eye failed to demonstrate that the difference in color is due to exposure. Finally, in two rabbits and in two dogs the lacrimal glands of one orbit were extirpated before the injection of blood. The blood patch looked pink as in human conjunctival hemorrhage only if the lacrimal gland was preserved; in eyes deprived of lacrimal irrigation, the blood patch turned bluish red on the third or fourth day, yellowish green two days later, and disappeared after the ninth day. The authors conclude that the bright red color of subconjunctival hemorrhage results from the formation of oxyhemoglobin; lacrimal fluid is needed to transfer oxygen to the blood deposit and to provide the temperature and hydroxyl-ion concentration essential for the oxygenation.

K. W. Ascher.

Bonazzi, A. **Giant conjunctival granuloma from vegetable foreign body.** Rassegna Ital. d'Ottal., 1947, v. 16, March-April, pp. 131-136.

The very large granuloma described was observed in a farmer whose left eye was injured at the age of a few months and had been atrophic since then. It was assumed that a vegetable foreign body, plus the irritation of the prosthesis, had excited the formation of the granuloma which was adherent at three points. The histologic sections showed nothing unusual. (3 figures.)

Eugene M. Blake.

Goldsmith, J. **New modification of the McReynolds transplantation for pterygium.** Arch. of Ophth., 1947, v. 37, Feb., pp. 194-198.

In the McReynolds operation, the sutures are passed blindly through the loose subconjunctival tissue to emerge from the conjunctiva. The looseness of the subconjunctival tissue does not predispose to firm adhesions with the head of the pterygium. When the silk sutures are removed on the third to the fifth day after operation, part of the newly-formed adhesion is usually disturbed and broken; and if the retractive pull of the pterygium is sufficiently powerful, it is not long before the neck and the head of the retracted pterygium align themselves in the horizontal meridian to commence invasion of the cornea again.

In the new modification, the pterygium is carefully dissected from the cornea and an incision made along the lower margin of the growth. A narrow tunnel is undermined in the bulbar conjunctiva below. An incision 5 mm. in length, concentric with the limbal curvature, is made into the bulbar conjunctiva and Tenon's capsule and is placed 5 mm. from the limbus and made to connect with the tunnel. The head of the pterygium is brought through the tunnel into the new incision and there under direct observation sutured to the episclera and Tenon's capsule with a 0000 chromic gut mattress suture. The chances of recurrence are reduced to a minimum. It is advisable to employ a traction suture if excessive tension on the head of the pterygium is anticipated. John C. Long.

Gutmann, M. J. **Allergic warm season conjunctivitis.** Acta Med. Orientalia, 1947, v. 6, May, pp. 167-169.

The symptoms of allergic conjunctivitis began to disappear 10 to 30 minutes after the intramuscular injection of 5 mg. riboflavin sodiumtetraborate and the patients were comfortable for 12 to 48 hours. Oral administration did not have the same effect.

Irwin E. Gaynon.

Lombardo, M. **Recession of limbal conjunctiva.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1109-1113. (4 figures, 1 table, references.)

Marin Amat, M., and Marin Enciso, M. **A profuse postoperative hemorrhage following a pterygium operation.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 389-391.

The authors report a postoperative hemorrhage after a pterygium operation, which assumed such proportions that it almost led to exsanguination, in spite of a compressive bandage, the use of all types of coagulants, and blood transfusion. The patient, a fifty-three-year-old woman, had had bilateral extirpation of the lacrimal sacs without complications three months previously. The pterygium operation with excision of the head was bilateral, and on the right side there was more than the usual bleeding during the operation. On the fourth postoperative day the right eye began to bleed after the bandage had been removed and the hemorrhage was checked by a compressive bandage. The bandage was removed the next day, and the following night the hemorrhage recurred, and continued for 24 hours in spite of all measures to arrest it. Hematologic studies revealed no basis for the bleeding. The authors attribute it to a K hypovitaminosis which resulted from chronic undernutrition. Ray K. Daily.

Peyret, J. A. **Vernal conjunctivitis: giant limbal type.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Oct.-Nov., p. 309.

The author reports a case of vernal conjunctivitis with unusually large limbal lesions. The diagnosis was confirmed by biopsy. Several methods of treatment were tried unsuccessfully. Finally radiotherapy improved the condition markedly, the improvement persisting throughout a period of observation of nearly five years.

Plinio Montalván.

Radnót, M. **A New oculo-glandular disease.** Ophthalmologica, 1947, v. 113, Feb., pp. 106-108.

Four cases of a conjunctival lesion are reported that occurred in patients who had contact with probably diseased poultry 24 hours before the onset of the symptoms. No bacteriological studies were made. The disease is probably caused by a virus. It occurred during an epidemic of "birds' plague" in Budapest (apparently an acute infectious disease of fowl similar to chicken cholera) and was characterized by swelling and hyperemia of the conjunctiva without secretion or corneal involvement, followed 24 hours later by the development of a painful preauricular lymphadenitis. Complete recovery occurred within a week.

Peter C. Kronfeld.

Zewi, M. **Reiter's disease.** Acta Ophth., 1947, v. 25, pt. 1, pp. 47-60.

Ten cases of Reiter's disease in patients treated at the Ophthalmic Clinic of the University of Turku are added to the literature. Whereas those formerly reported all occurred in adult men, six of the patients in this series were women. Two were 15 to 16 years old, and the others over 20. Seven of the patients presented the characteristic triad of polyarthritis, conjunctivitis, and urinary symptoms, and three had no urinary symptoms, which usually are slight and transient. All patients had arthritis, which healed completely. All patients had a catarrhal conjunctivitis which was the first ocular disturbance. Zewi finds that this conjunctivitis has distinguishing features not recorded heretofore, which are of diagnostic importance. The injection is deeper than in an ordinary conjunctivitis, and one has the impression that an episcleritis covers the visible area of the globe. Ten patients had in addition a superficial keratitis, one a mild optic neuritis, and one a keratitis, iritis, and optic neuritis. All recovered completely. Nine of the patients had had diarrhea before being taken ill. This has been reported before and there appears to be some relation between this disease and intestinal infection.

Louis Daily, Jr.

6

CORNEA AND SCLERA

Agnello, Francesco. **Herpes virus in the etiology of posttraumatic disciform keratitis.** Riv. di Oftalm., 1946, v. 1, Nov.-Dec., pp. 698-705.

Three cases of a posttraumatic deep corneal lesion are described. The lesion started three to four days after the injury, was unilateral and was associated with decreased sensitivity of the cornea and a tendency to recurrence. These qualities are characteristic of herpes. The injury was considered the precipitating etiologic factor and the basis of medicolegal action. K. W. Ascher.

Allen, J. A. **Antitoxin treatment of staphylococcic corneal ulceration.**

Amer. Jour. Ophth., 1947, v. 30, August, pp. 987-992. (4 figures, 3 tables, 2 references.)

Arjona, J. **Giant leproma of the sclerocorneal limbus.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 491-494.

A female patient, 36 years of age, had a tumor mass of six months duration on the left sclerocorneal limbus. It was a leproma and many Hansen's bacilli were found. The patient also had lepromas in the ears and on the hands.

J. Wesley McKinney.

Bedell, A. J. **Cephalosporium keratitis.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 997-1000. (5 figures, 20 references.)

Burki, Ernst. **Progress in keratoplasty.** Schweiz. Med. Wchnschr., 1947, v. 77, May 10, pp. 525-528.

This lecture gives the history of keratoplasty, its indications, present status and various techniques of applying it. Early attempts (1818) at transplanting animal corneas failed. v. Hippel, by introducing the round trephine was able to perfect the operation on man but as he too used animal tissue, he was not successful in obtaining clear transplants. Since 1906, when human tissue was first used, keratoplasty has grown constantly easier and more successful.

Methods of corneal transplants are divided into total and partial. So far total keratoplasty, desirable as it is, has not been successful. Partial keratoplasty is of two kinds, partial lamellar (superficial) and partial full thickness, of which the latter is the one in general use. The source of the transplant may be auto-, homo-, or heterogenous. The latter is no longer used. Autoplastic keratoplasty is the ideal procedure. A disc 6 to 8 mm. in diameter is cut out of a cornea with clear periphery and rotated so that the clear portion lies centrally. Healing leaves the cornea clear, but complications may result from the trepanation. Friede has recently suggested the use of a rectangular flap 3 to 4 by 8 mm. This reduces complications and will probably become the operation of choice.

Most ophthalmic surgeons prefer partial full-thickness homoplasty. A round flap, 3 to 5 mm. in diameter is preferred. Results are best after parenchymatous keratitis, injuries, and hereditary degenerations, poorest when there is anterior synechia or symblepheron or scarring from abscess or acid burns. Eyes with increased intraocular pressure are completely unsuited. The degree of injury is more important than the kind. Scars with anterior chamber intact are successfully replaced in 70 percent of cases, scars with anterior synechia in 20 percent. In complete leucoma the operation always fails. The degree of remaining visual acuity and age of patient are not decisive factors. Young children are less benefited than older individuals.

In homoplasty the donor material may be living cornea, surviving cornea, or killed cornea. The first can be available only in a very large clinic. The surviving cornea taken from patients recently dead of general disease is the material of choice. Eyes of older individuals are more suitable than those of the very young. The entire eye may be removed or pieces of cornea may be taken by trepanation. The material should be kept in a moist chamber at 4 to 6 degrees and may be thus stored for 10 to 12 hours. Transplants will remain clear for weeks if put into liquid paraffin, whereas salt solution

and other media quickly cause swelling and clouding. Tissue fixed in formalin will heal in, but always becomes cloudy later. Clouding is apt to occur eventually in many cases, and not until after eight months can one be certain that a transplant will remain clear. The factors causing late clouding are still unknown. Some believe the transplanted tissue remains and adapts itself as foreign tissue, others think the transplant is gradually replaced by the tissue of the host. Tissue regeneration unquestionably takes place since death and replacement of cells takes place constantly in all tissues.

B. T. Haessler.

Davidson, Alan. **Primary lipid dystrophy of the cornea.** Arch. of Ophth., 1947, v. 37, April, pp. 433-443.

A case of primary lipid dystrophy with hypercholesteremia in a 61-year-old negro is presented. The patient has been followed for 21 months, and the lesion in the left eye has progressed steadily and asymptomatically without evidence of inflammation.

A corneal transplantation was done on this eye, and pathologic studies of the transplant and of biopsy specimens of the cornea of both eyes revealed marked deposition of fatty globules in both corneas. Doubly refractile cholesterol crystals were seen in the epithelium of the left eye. The clinical characteristics of this condition are discussed. John C. Long.

Fox, Sidney A. **Removal of deeply embedded foreign bodies from the cornea.** Arch. of Ophth., 1947, v. 37, Feb., pp. 189-193.

Deep corneal foreign bodies may be removed by means of a corneal flap made with a Ziegler discission knife. The flap is fashioned by means of two incisions meeting at an apex pointing toward the center of the cornea and containing the foreign body between them. The incisions are beveled toward each other, so as to approach the foreign body more closely. After sufficient depth has been attained, the corneal flap is folded back on its base and the foreign body exposed and removed. Rust stains may be curetted. The corneal flap is patted back in place with a spatula. Six illustrative cases are described. John C. Long.

Franceschetti, S., and Babel, J. **Histologic examination of a transparent corneal implant.** Ann. d'Ocul., 1947, v. 180, March, pp. 142-146.

Exactly how transparent corneal implants remain viable is not understood. One half of an eye containing a corneal graft which had been transparent during six years was imbedded in paraffin and sectioned longitudinally; the other half was stained with silver and cut frontally for better study of the corneal nerves. Sections showed that Bowman's membrane was present in the implant but not in the host. Descemet's membrane was present both in the host and the implant but was interrupted at their junction. No new vessels were observed in the implant and the stromal layers were continuous with those of the host. Numerous nerves which branched dichotomously were observed in the recipient cornea. Some of the nerves on passing toward the implant made a loop at its border and then entered the recipient cornea parallel to the implant margin. The nerves in the graft were subepithelial.

The primitive structure of the transplant was preserved. Cellular elements pass from the host into the graft. Nerve innervation is apparently secondary to vascularization. Nerve filaments in the

epithelium possibly have a trophic action essential to the physico-chemical exchange which is necessary in maintaining corneal transparency. (7 figures, 7 references.) Chas. A. Bahn.

Katzin, H. M. **The preservation of corneal tissue by freezing and dehydration.** Amer. Jour. Ophth., 1947, v. 30, Sept., pp. 1128-1134. (1 table, 23 references.)

Krawicz, T. **The reticulo-endothelial system of the cornea.** Brit. Jour. Ophth., 1947, v. 31, July, pp. 421-423.

To investigate the colloidopectic properties of corneal cells, that is, their permeability to colloidal substances, various dyes were dropped into the conjunctival sac of 30 rabbits for 50 days.

Ten rabbits were similarly treated with solutions of colloidal silver. In microscopic sections the dyes were found in all layers of the cornea which simply acted as a semipermeable membrane between the dye and the anterior chamber. The silver deposits were found intracellularly within the stromal cells and more abundantly within the structure of Descemet's membrane. The author concludes that the corneal stroma cells are wandering cells in a state of rest which means that they correspond to prohistiocytes and that they do not differ functionally from the fundamental components of the reticulo-endothelial system.

Morris Kaplan.

Langer, Z. M. **Therapeutic keratoplasty in purulent keratitis.** Oftal. Jour. (Odessa), 1946, pt. 3, pp. 34-36.

This is a report of 12 apparently hopelessly lost eyes with extensive traumatic purulent keratitis, with visual acuity ranging from faulty light projection to hand movements, treated by keratoplasty. In two fresh cornea was used for transplantation, and both eyes were lost. In ten eyes preserved cornea was used, and the final results were form vision in three, hand movements in one, and light perception in six. Regression of the inflammatory phenomena was apparent in two to three days after the operation. The postoperative course was complicated in 9 eyes by anterior synechia and secondary glaucoma. A prophylactic iridectomy, performed while the eye was acutely inflamed, was always beneficial. The curative effect of the transplant is believed to be due to its content of biogenic stimulators. The resulting corneal leucoma can be dealt with later by an optical keratoplasty.

Ray K. Daily.

Manschot, W. A. **Blood staining of the cornea.** Ophthalmologica, 1947, v. 113, April, pp. 203-214.

Four eyes with blood staining of the cornea became available for histologic examination. In one eye the staining occurred as a result of an obstruction of the central retinal vein with secondary glaucoma; in the other three eyes the staining developed after severe trauma. In two of the eyes the staining had been present only for a few days, in the other two eyes for several months. In the histologic picture different stages of the process can be distinguished. The first stage is characterized by the presence of the blood as an amorphous mass between the lamellae. After a few days this amorphous mass takes on a granular form, and then, apparently as the result of absorption from these interlamellar granules, the well-known highly refractile bodies of blood staining develop within the lamellae (second stage). This form of blood staining can last very long. The opaque disc in the

center of the cornea becomes smaller as time goes on, but a small central opacity is the usual permanent result of blood staining. The author has studied histologically the pigment particles that remain within the corneal corpuscles and found them to contain iron as well as fat (hemosiderin as well as lipofuscin). In a fifth (injured) eye the author was able to determine the chemical nature of the highly refractile bodies. After fixation in saturated mercury bichloride, he subjected the sections to tryptic digestion at 37° centigrade. Within seven days the refractile bodies disappeared from the sections which proves that they consist of proteins, apparently the crystalline form of the protein part of the hemoglobin molecule. Peter C. Kronfeld.

Nataf, R., and Fontan, P. **Hereditary familial megalocornea.** Ann. d'Ocul., 1947, v. 180, May, pp. 267-272.

In a 20 year old male, both corneas were 14 to 16 mm. in diameter, globular and transparent and associated with iridodonesis. Vision could be corrected to 7/10 in each eye. The fields and color vision were normal. Embryotoxon was observed in each eye and in the right there was opacification of the lens nucleus, slight coloboma of the lens above, and partial absence of the zonula. The anterior chamber angle was free but distended. In both eyes the tension was 25 mm. Hg. No apparent endocrine disturbance existed, and the blood Wassermann reaction and chemical test of the blood were negative. Megalocornea existed in the maternal grandfather and in one brother. Chas. A. Bahn.

Pascheff, C. **Further research on pannus follicularis trachomatosus.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 1001-1004. (4 figures, 8 references.)

Peyret, J. A. **Familial corneal dystrophies.** Arch. de Oft. de Buenos Aires, 1946, v. 21, Aug., p. 205.

Two cases of Groenow's corneal dystrophy in mother and son are reported. In the first, a nuclear cataract was extracted from the right eye without complications. The vision improved to 1/10 with correction.

The literature on the subject is briefly reviewed. (Illustrations, bibliography.) Plinio Montalván.

Sagher, F., and Miterstein, B. **Effect of Grenz rays on leprous infiltrates.** Arch. of Ophth., 1947, v. 38, July, pp. 78-88.

Grenz rays were applied to lepromatous changes in the anterior segments of the eyeball in six patients. Since it was obvious, on the basis of experience with irradiation of the skin, that only large doses would be able to produce an effect, three practically sightless eyes were chosen for exposure to these rays. In all three patients the lepromas undoubtedly became reduced in size or disappeared completely.

When the Grenz rays were employed on the eyes of three additional patients which presented lepromas with fairly good vision, two eyes exhibited a favorable response, whereas in the third the lepromatous part which was irradiated became quiescent, or even slightly flatter, but the surrounding parts presented rapid growth of new lepromas.

The voltage of the rays used ranged from 6 to 14 kilovolts, which is equivalent to half value layers of 0.021 to 0.031 mm. of aluminum. The most effective doses applied at one sitting were from 700 to 1,200 r, and the total amount varied from 5,500 to 11,600 r. These large doses could be applied safely to the external tissues of the eye because the sensitivity of such tis-

sues to rays is lower than that of the skin. No damage to the cornea, lens or deeper structures of the eye was noted, so far as this could be determined on the basis of observations extending over a period of two to four years.

R. W. Danielson.

Schmidtke, R. L. **Hypovitaminosis A in ophthalmology.** Arch. of Ophth., 1947, v. 37, May, pp. 653-667. (See Section 17, Systemic disease and parasites.)

Shepard, E. M. **Relief of episcleritis by histamine diphosphate.** Amer. Jour. Ophth., 1947, v. 30, July, pp. 907-909.

Sjønoft, Finn. **A case of interstitial keratitis after a gluteal abscess.** Acta Ophth., 1947, v. 25, pt. 1, pp. 73-80.

The gluteal abscess developed as a result of a milk injection given for a slight bilateral iridocyclitis, and cultures of the abscess showed hemolytic streptococci. Thirteen days after the milk injection a bilateral symmetrical corneal affection developed, which began near the limbus above, and gradually spread toward the center, with disseminated grayish interstitial foci. Myocarditis and pulmonary abscess developed on the day following the onset of the keratitis. In the course of 54 days, during which several fresh corneal foci appeared, the infiltrates disappeared, becoming hazier and receding towards the limbus. The patient was dismissed with residual posterior synechia, and small deep peripheral corneal opacities with deep vascularization. It was thought that the patient had a metastatic parenchymatous keratitis, secondary to a sepsis caused by the streptococcus. Where the streptococci originated remained undertermined. It is not believed that it originated in the milk, because another patient, who was injected with 10 cc. of the same portion of milk suffered no complications.

Louis Daily, Jr.

Stanbury, F. C., and Wadsworth, J. A. C. **Surgical technique of corneal transplantation in rabbits.** Amer. Jour. Ophth., 1947, v. 30, August, pp. 968-978. (6 figures, 19 references.)

Valdecasas, Pedro G. **Keratitis caused by an alcoholic solution of chirimoya seeds.** Arch. de la Soc. Oft. Hisp.-Amer., 1947, v. 7, April, pp. 379-380.

Valdecases believes that the cases of keratitis reported by Romero as caused by alcohol fumes from a shampoo, are actually due to the caustic effect of chirimoya seeds, commonly steeped in alcohol, and believed to be effective against head lice. At present alcohol is commonly used as a constituent of face lotions and colognes, and it seems improbable that it alone could produce as pronounced corneal damages as was found in Romero's cases. It is more probable that the offending agent was the macerated seeds; the greater involvement of the center of the cornea is attributed to the lesser humidity in that area, which diminishes its capacity to neutralize the caustic effect of the alcoholic solution of these seeds.

Ray K. Daily.

7

UVEAL TRACT, SYMPATHETIC DISEASE, AND AQUEOUS HUMOR

Arentsen, Juan. **A case of sympathetic ophthalmia cured with penicillin.** Arch. Chilenos de Oft., 1946, v. 2, July-Oct., pp. 249-255.

The author has devoted attention to subconjunctival treatment with peni-

cillin, and arrives at the conclusion that the doses employed were in many cases too low. When the dose was carried above 1,000 or 1,500 Oxford units, the injections became very painful, so preliminary injection of 2-percent novocaine solution subconjunctivally was resorted to, and in this way it was possible to raise the dose of penicillin to 5,000 units. The author regards the best combination for subconjunctival injection as one part of 4-percent novocaine solution with two parts of physiologic sal solution that contains 5,000 Oxford units of penicillin per cubic centimeter. He reports the favorable outcome of such treatment in a sympathizing eye in which the involvement persisted for some time after removal of the exciting eye. W. H. Crisp.

Barahona, B. **Ectropion of the uvea.** Arch. de la Soc. Oft. Hisp.-Amer., 1946, v. 6, May, pp. 494-496.

A case of congenital ectropion of the uvea in a girl five years old is reported. The ectropion covered a large part of the iris stroma. The eye showed no other anatomic or function anomaly. J. Wesley McKinney.

Carusi, E. **A new procedure for the treatment of iridodialysis.** Rassegna Ital. d'Ottal., 1947, v. 16, March-April, pp. 93-97.

The procedure described consists of four steps. The conjunctival flap is dissected at the site of the iridodialysis; a keratome is introduced one half millimeter from the limbus to make an incision slightly less than the width of the dialysis; the iris is caught on a Jaeger hook and drawn out of the wound for one millimeter. The iris is then transfixed with a double-armed suture of hair by passing the needles through the conjunctival flap and tying the knot. The iris is gently replaced so that the pupil is as nearly round as possible. Finally, the conjunctival flap is sutured with interrupted silk sutures. Eugene M. Blake.

Dragomiretzki, G. A. **Therapy of myopic chorioretinitis with vitreous from preserved eyes.** Oftal. Jour. (Odessa), 1946, pt. 3, pp. 32-33.

Dragomiretzki experimented with rectal and subcutaneous injections of autoclaved vitreous of preserved beef eyes. The course of therapy consisted of 10 injections, every other day. The tabulated data of 12 cases show an improvement in visual acuity, and in five patients a 10 to 15-degree widening of the visual fields. Ray K. Daily.

Gormaz, Alberto. **Sympathetic ophthalmia.** Arch. Chilenos de Oft., 1946, v. 2, July-Oct., pp. 255-256.

The author reports a case in which sympathetic involvement of the second eye began 56 days after enucleation of the exciting eye. Recovery occurred under sulfathiazole. W. H. Crisp.

Kholina, A. A. **Tissue therapy with the Filatov method.** Oftal. Jour. (Odessa), 1946, pt. 3, pp. 29-31.

Kholina reports from Kiev nine cases of severe iritis, which recovered more rapidly than usual, under treatment with injections of extract of leaves of aloes, and implantation of preserved skin. Ray K. Daily.

Matteucci, P. **Sympathetic innervation and the neuro-vegetative regulation of the uvea. (Influence of the cervical sympathetic upon intraocular tension in normal and pathological eyes.)** Rassegna Ital. d'Ottal., 1947, v. 16, May-June, pp. 186-198.

The conclusions reached by the author are derived from experiments upon rabbits and from histologic studies of the eyes which were enucleated after the experiments. Interference with the sympathetic nerves provokes oscillations of ocular tenion without modifying the caliber of the choroidal vessels. It also disrupts the physico-dynamic circulatory equilibrium of the blood and aqueous, so that there is altered capillary permeability and retarded reformation of the aqueous after puncture of the anterior chamber. Pigmentary changes were observed in the iris and ciliary processes. (9 photomicrographs.) Eugene M. Blake.

Morano, M. **Detachment of choroid in the course of hypertensive toxemia of pregnancy.** Boll. d'Ocul., 1946, v. 25, July-Sept., pp. 379-401.

Systematic observations of the fundus during eclampsia or the pre-eclampsia state, four cases of which are described in detail, lead the writer to believe that the so-called retinal detachment of eclampsia is in reality a detachment of the choroid. The sudden bilateral appearance of dark-gray nonfluctuating protrusions of the retina, always in the lower portion, the lack of retinal tears, and the disappearance of the protrusions after the emptying of the uterus are considered typical differential symptoms. Especially important for the differential diagnosis is the presence of pigment changes at the site of the detachments and the choroidal atrophy as is seen in choroidal detachment after intraocular operations such as cataract extractions and decompressive procedures. The pathogenesis of similar detachments is discussed at length. (Bibliography.)

Melchiore Lombardo.

Nyquist, B. **Benign course of sympathetic ophthalmia.** Acta. Ophth., 1947, v. 25, pt. 1, pp. 9-17.

Four cases of transient sympathetic ophthalmia, designated as such by Meller in 1925, are briefly reported. Three cases followed perforating sclero-corneal injuries, and one a cataract extraction. Two of the eyes were perforated by metallic splinters which entered the eyeball, and were extracted with a magnet, and one cornea was perforated by a piece of wood. All of the sympathizing eyes were free from subjective symptoms and had no ciliary congestion. The diagnosis was based on the presence of a few circulating corpuscles in the aqueous, and one or several small deposits on the posterior corneal surface, found on routine slit-lamp examination. Treatment during the pre-sympathetic stage consisted of atropin, pyrogenic agents, and rest. After the onset of sympathetic ophthalmia mercury ointment, neoarsphenamine, X-ray therapy, reduced illumination, and prolonged bed-rest were added. Of three enucleated eyes, histologic examination was available in two; the sections showed a chronic uveal inflammatory process, without typical nodules or giant cells. It is believed that intensive therapy arrested the development of the anatomic changes typical of sympathetic ophthalmia. The question of enucleating the injured eye after the appearance of sympathetic ophthalmia in the fellow eye is discussed, and contrary to the general belief Nyquist holds that such eyes should be enucleated because the inflammatory process in the injured eye may cause relapses of sympathetic ophthalmia in the fellow eye. (4 photomicrographs.)

Louis Daily, Jr.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
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News items should reach the editor by the 12th of the month

DEATHS

Dr. William Lorne Deeton, Cleveland, Ohio, died July 28, 1947, aged 47 years.

Dr. James Garfield Dwyer, New York, New York, died August 2, 1947, aged 65 years.

Dr. Edwin Baker Goodall, Boston, Massachusetts, died August 6, 1947, aged 65 years.

Dr. John Jacob Gurtov, New York, New York, died July 28, 1947, aged 67 years.

Dr. Joseph Hallock Moore, Huntington, West Virginia, died August 3, 1947, aged 45 years.

Dr. Alpheus Keller Wilson, Jacksonville, Florida, died July 24, 1947, aged 67 years.

MISCELLANEOUS

During September and October, the Department of Ophthalmology, University of Glasgow, held a series of postgraduate lectures. The following papers were read and discussed: "Contact Lenses," Mr. F. Ridley; "Industrial Cataract," Dr. J. D. Fraser; "Pathology and Clinical Aspects of Ocular Glassmembranes," Prof. Arnold Loewenstein; "Some Problems in Ophthalmoscopic Diagnosis," Prof. A. J. Ballantyne; "Ophthalmology in Poland," Prof. W. J. B. Riddell.

SOCIETIES

PRELIMINARY PROGRAM

III PAN-AMERICAN CONGRESS

A tentative program for the III Pan-American Congress of Ophthalmology, at Havana, Cuba, has been announced by the committee.

Sunday—January 4, 1948

8:30 a.m.—Registration
3:00 p.m.—Preparatory Assembly—(business)
5:00 p.m.—Opening of Exposition—(scientific & commercial)
9:30 p.m.—Formal opening at Capitol

Monday—January 5, 1948

8:30 a.m.—Official opening of Scientific Program
12 to 2 p.m.—Lunch
2:00 p.m.—Official subjects of Scientific Program
9:00 p.m.—Formal session—University—(Honoring the Rector of the University of Havana, the Dean of Faculty of Medicine, and the Guest of Honor.)

Tuesday—January 6, 1948

8:30 a.m.—Official subjects of Scientific Program
12 to 2 p.m.—Lunch
2:00 p.m.—Courses—English, Portuguese, Spanish
4:30 p.m.—Exhibits
6:30 p.m.—Reception by the Mayor of Havana
9:30 p.m.—Cuban fiesta

Wednesday—January 7, 1948

8:30 a.m.—Official subjects of Scientific Program
12 to 2 p.m.—Lunch
2 to 4:30 p.m.—Courses—English, Portuguese, Spanish
7:00 p.m.—Reception by the Cuban Medical Federation
9:00 p.m.—Formal session Academy of Science—Gradle Lecture—Prevention of Blindness Medal to Dr. Harry S. Gradle—Award of Pan-American Medals

Thursday—January 8, 1948

8:30 a.m.—Official subjects of Scientific Program
12 to 2 p.m.—Lunch
2 to 4 p.m.—Courses—English, Portuguese, Spanish
4:00 p.m.—Free papers
9:30 p.m.—Pan-American fiesta at the Havana Yacht Club

Friday—January 9, 1948

8:30 a.m.—Official subjects of Scientific Program
12 to 2 p.m.—Lunch
3:00 p.m.—Business meeting
6:00 p.m.—Reception at the President's Palace

Saturday—January 10, 1948

8:30 a.m.—Prevention of Blindness
1:30 p.m.—Lunch at the Jockey Club
2:30 p.m.—Races
9:00 p.m.—President's banquet—(Closing)

ANNOUNCEMENT

BOARD EXAMINATIONS

The American Board of Ophthalmology announces that the written qualifying test will be given on January 14, 1948, in many cities throughout the country. Practical examinations will be given at Baltimore in May, and at Chicago in October. Information may be obtained from Dr. S. Judd Beach, secretary, 56 Ivie Road, Cape Cottage, Maine.

PAN-AMERICAN NOTES

Edited by M. Uribe Troncoso, M.D., 500 West End Avenue, New York

Communications should reach the editor by the 12th of the month.

III Pan-American Congress of Ophthalmology

The government of Cuba has extended official invitations to all the governments of America to send representatives to the III Pan-American Congress of Ophthalmology. It is expected that many ophthalmologists will be present, not only from this country, but also from South America and Europe. Sir Stewart Duke-Elder, London, Dr. Bailliart, Paris, Dr. A. Fuchs, China, Dr. Manuel Marquez formerly of Madrid and now of Mexico City, Dr. K. Lindner, Vienna, and Dr. H. Arruga, Barcelona, have promised to attend and read papers. Besides the official reports, 27 free papers have been included in the program. In a special session on January 7th an honor medal of the Pan-American Congress will be presented to Dr. William H. Crisp of Denver and Dr. Manuel Uribe Troncoso of New York.

The meeting of January 10th will be devoted to papers and discussions on prevention of blindness, in which Dr. F. M. Foote from the United States and other directors of similar societies in Latin America will be present. Dr. P. Bailliart, the president of the International Association for the Prevention of Blindness, has promised to attend the meeting.

Fifty courses of instruction given in English, Spanish, and Portuguese are included in the program and will take place on January 6th, 7th, and 8th. Besides the Scientific Exhibition there will be a Technical Exposition and an Exhibition of Ophthalmological Literature. A new departure is the collection of amateur art, curiosities, oil and water color paintings, photographs, sculptures, and other objects of similar nature made by ophthalmologists or their relatives.

The receptions and entertainments will be numerous. The President of the Cuban Republic will receive the members of the Congress in the Presidential Palace and the many social and medical clubs of Havana will be open to all members and their families.

Although no more reservations are available at the principal hotels, the local committee, (Dr. Miguel Branly, Secretary Escuela de Medicina, Calle 25 e I, Vedado, Habana) is arranging to provide new accommodations for late applicants in the smaller hotels and in private houses. A check or money order for ten dollars ($10.00) should be sent to the secretary to secure reservations.

Guatemalan Ophthalmological Society

On August of this year on the occasion of the visit of Dr. Tomas R. Yanes and Dr. M. A. Branly of Habana, the ophthalmologists of Guatemala met and started a society which will work for the advancement of ophthalmology in the country and encourage the education of young specialists. Dr. Branly offered a fellowship in ophthalmology for a student who will attend the courses in Habana University and its Hospital. On the board of the society are Dr. R. Pacheco Luna, president, and Dr. J. Miguel Medrano, secretary.

Necrology

Dr. A. Garcia Miranda, professor of ophthalmology in Granada and then in Salamanca, Spain, one of the most progressive young Spanish ophthalmologists, died recently in Spain, after a professional trip to the United States.

Chile

At a meeting held on April 5, 1946, the following officers were unanimously elected by the Sociedad Chilena de Oftalmologia: President, Prof. Italo Martini; vice president, Prof. C. Espildora Luque; treasurer, Dr. Rene Contardo; secretary, Dr. Adrian Araya; pro-secretary, Dr. Herman Brink.

Ecuador

The Sociedad Ecuatoriana de Otorrinolaringologia y Oftalmologia (Quito) has elected the following officers: President, Dr. L. Fernando Lopes; vice president, Dr. Herman Parker; secretary, Dr. A. Carlos Peña; treasurer, Dr. P. Cevallos Jijon.

Uruguay

The Sociedad Uruguaya de Oftalmologia has elected the following officers to serve during 1946-47: President, Dr. Julio A. Sicardi; vice president, Dr. Luis A. Barriere; secretary, Dr. Guillermo Rivas; treasurer, Dr. Ignacio Errea.

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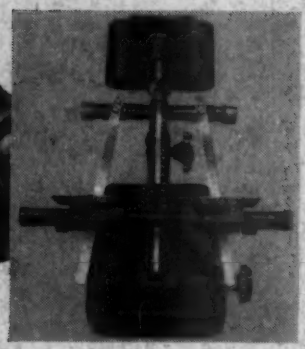

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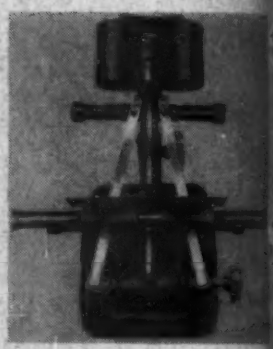

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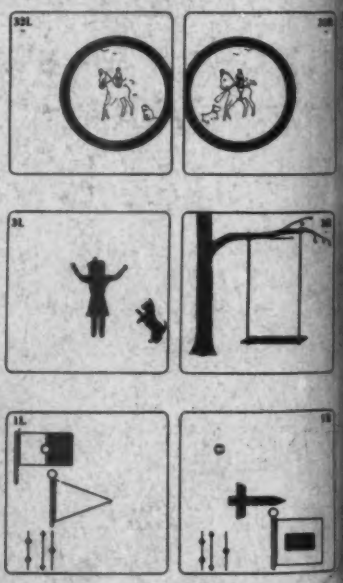

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